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(54) Title: BIOCHEMICAL MARKERS OF THE HUMAN ENDOMETRIUM		
(57) Abstract Assay methods are provided for detection or quantitation of any of several proteins which are specifically produced in the endometrium in association with hyperplasia, adenocarcinoma or the proliferative phase of the endometrium. The relevant proteins have been identified by 2D gel electrophoresis with subsequent sequence identification by mass spectroscopic finger printing of tryptic digests.		

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BIOCHEMICAL MARKERS OF THE HUMAN ENDOMETRIUM

The endometrium is the mucous lining of the uterine cavity. During the menstrual cycle, the endometrium is the organ in the body that shows the greatest changes under the influence of the sex hormones, oestradiol and progesterone. In the oestrogen dominated phase the endometrium proliferates until progesterone from the corpus luteum transforms the oestrogen-primed proliferative endometrium to a secretory phase endometrium. In due course this is followed by shedding of the fully transformed endometrium during the menstruation, and a new cycle will begin.

Persistent unbalanced oestrogen stimulation either due to increased endogenous production of oestrogens, or replacement therapy in which oestrogens are given alone, is associated with increased risk of developing endometrial hyperplasia and subsequently endometrial adenocarcinoma. Histologically, these pathological conditions are characterised by increased thickness of the endometrium and irregular pattern of the endometrial glandular cells.

Endometrial adenocarcinoma is a life threatening condition.

At present the endometrial status is assessed by histological and biochemical analysis of endometrial biopsies. This is time-consuming, expensive and causes discomfort for the woman. It would be highly desirable to identify biochemical markers which could be measured in body fluids reflecting the endometrial status, obviating the need for endometrial biopsies. The detection of such markers in histological samples would also however be advantageous as an additional method of recognising the histological status of such samples.

We have now discovered that certain proteins are produced in the endometrium in increased amounts associated with hyperplasia and that certain proteins are produced in increased amounts associated with adenocarcinoma. These two groups of proteins overlap somewhat. The present invention relates in a first aspect to such proteins and to their diagnostic uses.

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Unless otherwise indicated, references to the proteins herein include references to modified forms of the proteins and derivatives of the proteins, including but not restricted to glycosylated, phosphorylated, acetylated, methylated or lipidated forms thereof.

Thus the invention provides a method of characterising a biological sample comprising detecting or quantitating therein one or more proteins produced by the endometrium in increased amounts in hyperplasia or in adenocarcinoma as shown by 2D gel electrophoresis comparison of cell lysates of endometrial biopsies from normal endometrium and endometrium showing hyperplasia or adenocarcinoma, excluding variations due to the menstrual cycle, or detecting or quantitating a fragment or breakdown product thereof, or a nucleic acid coding therefor, or an antibody thereto.

The invention includes a method of characterising a biological sample comprising detecting or quantitating therein one or more proteins produced by the endometrium in increased amounts in hyperplasia or in adenocarcinoma and characterised by one of the following combinations of molecular weight and pI values:

hyperplasia		
	pI	MW kDa
25	6.7	91
	6.6	90
	6.9	64
	6.6	67
	6.3	66
30	6.8	46
	5.7	41
	5.5	35
	5.3	13
	6.6	101
35	5.8	14
	7.4	51
	8.2	44
	9.5	48

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	adenocarcinoma	
	pI	MW (kDa)
5	6.3	32
	6.0	109
	6.7	91
	6.6	90
10	6.9	64
	6.6	67
	6.3	66
	6.2	62
	6.2	45
15	5.7	45
	5.4	33
	6.3	27
	6.5	103
	6.8	90
20	6.9	78
	5.3	13
	6.2	130
	6.3	66
	6.3	73
25	8.3	32
	8.1	55
	8.2	44
	6.6	111
	7.7	43
30	9.5	48
	8.3	32
	7.7	39

or a fragment or breakdown product thereof, or a nucleic
 35 acid coding therefor, or an antibody thereto.

Said protein, fragment, breakdown product, antibody or
 nucleic acid may preferably be detected in a body fluid
 sample but may also be detailed in other forms of sample
 such as histological samples or cytological samples.

The invention includes an immunological binding partner specifically reactive with a protein as defined above with a
5 fragment or breakdown product thereof or with a nucleic acid coding therefor.

It also includes a cell line producing a monoclonal antibody being such an immunological binding partner.

The invention includes also an assay kit for use in
10 such an analysis method comprising an immunological binding partner as described.

This aspect of the invention has resulted from studies aiming to detect endometrial proteins with increased synthesis in endometrial adenocarcinoma as compared to the
15 synthesis during the normal menstrual cycle; to detect endometrial proteins with increased synthesis in endometrial hyperplasia as compared to the synthesis during the normal menstrual cycle; and to detect proteins showing a cycle-related expression during the normal menstrual cycle.

20 In a second aspect the invention relates to the discovery of markers of the "proliferative" phase of the human endometrium. A protein marker for the "secretory" phase of the endometrium has been previously described, see US-A-4,489,166. No similar marker has been described for
25 the proliferative phase although certain candidate proteins were described in Ref. 1.

Under influence of the sex hormones, oestradiol and progesterone, the human endometrium undergoes cyclical variation with an oestrogen-dominated phase, i.e. the
30 proliferative phase, an ovulation phase, i.e. the interval phase, a progesterone-dominated phase, i.e. the secretory phase, and finally the endometrium is shed, i.e. the menstrual phase. The same cyclical variation of the endometrium is seen in postmenopausal women receiving
35 sequentially combined hormone replacement therapy. The demand for endometrial status assessment has highly increased in the latest decade, not only on account of the extensive research into fertility, but also in order to

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estimate endometrial response to the large number of combined oestrogens/progestogen preparations used in hormone replacement therapy. It would be highly desirable to identify biochemical markers which could be measured in body fluids reflecting the endometrial status, obviating the need for endometrial biopsies. Studies have suggested that serum placental protein 14 (PP14), which is produced in the glandular cells of the secretory phase endometrium (Ref. 3), is a reliable marker of the secretory phase endometrium. It has been shown that serum PP14 strongly correlates with the secretory activity of the endometrium in postmenopausal women receiving hormone replacement therapy (Ref. 4,5). No similar marker exists for the proliferative phase endometrium.

We have now discovered that certain proteins are produced in the endometrium in increased amounts in proliferative phase endometrium as compared to secretory phase endometrium.

According to this aspect of the invention there is now provided a method of characterising a biological sample comprising detecting or quantitating therein one or more proteins produced by the endometrium in increased amounts during the proliferative phase of the endometrium as shown in 2D gel electrophoresis comparison of cell lysates of endometrial biopsies from normal endometrium in its proliferative and secretory phases and characterised by one of the following combinations of molecular weight and pI values:-

pI	MW (kDa)
6.9	86
5.4	34
5.6	67
5.3	23
6.8	52
8.7	47
8.2	138
6.5	124
7.7	119
7.8	119
8.1	66
7.1	59
6.8	66
7.9	48
7.7	31
6.8	29
7.2	70
8.0	119
6.7	62

or a fragment or breakdown product thereof, or a nucleic
5 acid coding therefor or an antibody thereto.

Such a method may preferably be for detecting the phase
of the endometrium.

The preferred features of the first aspect of the
invention apply also to this second aspect.

10 This aspect of the invention includes a method of
determining the proliferative/secretory phase status of the
endometrium comprising the quantitative or qualitative
measurement in a sample of any one or more of the proteins
defined above or a breakdown product or fragment thereof.

15 It also includes an immunological binding partner for any of
the said proteins, breakdown products or fragments or a cell
line producing such a binding partner.

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Whilst the sequences and properties of proteins discussed above relate to human proteins, the assay procedures of the invention may be practised on samples arising from other species. Especially in this context, references to proteins herein should be understood to include proteins having a degree of homology of at least 60% with the given amino acid sequences irrespective of any modifications of said amino acids. When determining homology, modified amino acids such as phosphorylated, acetylated, amidated, methylated, glycosylated or lipidated derivatives of an amino acid should thus be considered to be the same as the amino acid without any such modification. Such peptides may be derived from similar proteins from other species, e.g. other mammals such as mouse, rabbit, guinea pig, pig, or cow or may be entirely or predominantly of synthetic origin.

The degree of homology may be advantageously be at least 65%, or at least 70%. Under certain circumstances, it is advantageous that the degree of homology is even higher such as at least 80% or at least 90%. Other DNA sequences which encode substantially the same amino acid sequence as a gene encoding a marker protein, i.e. a marker gene, may be used in the practice of the present invention. These include, but are not limited to, allelic genes and homologous genes from other species.

Nucleic acid fragments comprising a nucleotide sequence which codes for a protein described above or a peptide derived from it as well as nucleic acid fragments which hybridise with these nucleic acid fragments or a part thereof under stringent hybridisation conditions, e.g. 5 mM monovalent ions (0.1xSSC), neutral pH and 65°C are important aspects of the invention. The term "highly stringent", when used in conjunction with hybridisation conditions, is as defined in the art, i.e. 5-10°C under the melting point T_m , cf, Sambrook et al, 1989, pages 11.45 - 11.49.

By the term "nucleic acid" is meant a polynucleotide of high molecular weight which can occur as either DNA or RNA and may be either single-stranded or double-stranded.

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Once the amino acid sequences of the proteins of utility in the present invention are known, it is possible to synthesise DNA or RNA probes which may be used for:

- 5 i) direct detection of DNA and RNA expressing said proteins on a fixed or frozen tissue section using, e.g. chromogenous, chemiluminescent or immunofluorescent techniques;
- ii) polymerase chain reaction (PCR) or other amplification techniques; and
- 10 iii) locating the part or all of the gene, isogene, pseudogene or other related genes either in cDNA libraries, genomic libraries or other collections of genetic material from either the host or other animals, including man.

15 In another aspect, the invention relates to a binding means which specifically binds to a relevant protein or peptide or nucleic acid fragment as described above. In particular, the invention relates to an antibody which specifically binds to a relevant protein or peptide or an
20 antigen-binding fragment thereof, i.e. a polyclonal antibody, a monoclonal antibody, chimeric antibody, single chain antibody fragment, Fab and Fab' fragments, and an Fab expression library.

 It is contemplated that both monoclonal and polyclonal
25 antibodies will be useful in providing the basis for one or more assays to detect relevant peptides and proteins. Antibodies which are directed against epitopes that are specific for the proteins will be most useful as cross reaction will be minimised therewith.

30 Based upon the identification of relevant proteins described above, assay methods and kits may be produced according to standard methodology. Thus, the proteins may be obtained in purified form, either by extraction from tissues or by synthesis, and antibodies may be raised
35 thereto or to characterising peptide sequences thereof. Standard assay formats employing such antibodies may be utilised according to the invention.

Preferred immunoassays are contemplated as including various types of enzyme linked immunoassays (ELISA), immunoblot techniques, and the like, known in the art.

5 However, it is readily appreciated that utility is not limited to such assays, and useful embodiments including RIAs and other non-enzyme linked antibody binding assays or procedures. The proteins themselves or peptides derived from the protein sequences may be used in detecting auto-

10 antibodies to such proteins.

Samples of the proteins described above have been subjected to trypsin digestion and the molecular weight of the resulting fragments has been determined by mass spectrometry. This provides a "fingerprint" of the protein

15 which can be matched to date in established data bases available to those working in this field. This procedure has enabled us to identify certain of the proteins as being previously known in other contexts. No matches have been found for certain others, indicating that they have not

20 previously been known.

The invention will be illustrated and explained further by the following description in which the Figures as follows:-

25 Figure 1: Fluorograph of a two-dimensional gel electrophoresis of [³⁵S]methionine labelled endometrial proteins separated in the first dimension by iso-electric focusing (IEF; pI 3.5-7) and in the

30 second dimension by sodium dodecyl sulphate polyacrylamide gel electrophoresis. The locations of the spots with increased synthesis in hyperplasia are indicated.

Figure 2: Fluorograph of a two-dimensional gel electrophoresis of [³⁵S]methionine labelled endometrial

35 proteins separated in the first dimension by non-equilibrium pH gradient gel electrophoresis (NEPHGE; pI 6.5-11) and in the second dimension by sodium dodecyl sulphate polyacrylamide gel

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electrophoresis. The locations of the spots with increased synthesis in hyperplasia are indicated.

Figure 3: Fluorograph of a two-dimensional gel electrophoresis of [³⁵S]methionine labelled endometrial proteins separated in the first dimension by isoelectric focusing (IEF; pI 3.5-7) and in the second dimension by sodium dodecyl sulphate polyacrylamide gel electrophoresis. The locations of the spots with increased synthesis in adenocarcinoma are indicated.

Figure 4: Fluorograph of a two-dimensional gel electrophoresis of [³⁵S]methionine labelled endometrial proteins separated in the first dimension by nonequilibrium pH gradient gel electrophoresis (NEPHGE; pI 6.5-11) and in the second dimension by sodium dodecyl sulphate polyacrylamide gel electrophoresis. The locations of the spots with increased synthesis in adenocarcinoma are indicated.

Figure 5: Fluorograph of a two-dimensional gel electrophoresis of [³⁵S]methionine labelled endometrial proteins separated in the first dimension by isoelectric focusing (IEF; pI 3.5-7) and in the second dimension by sodium dodecyl sulphate polyacrylamide gel electrophoresis. The locations of the spots with increased synthesis in proliferative phase endometrium are indicated.

Figure 6: Fluorograph of a two-dimensional gel electrophoresis of [³⁵S]methionine labelled endometrial proteins separated in the first dimension by nonequilibrium pH gradient gel electrophoresis (NEPHGE; pI 6.5-11) and in the second dimension by sodium dodecyl sulphate polyacrylamide gel electrophoresis. The locations of the spots with increased synthesis in proliferative phase endometrium are indicated.

Figure 7: Tryptic digestion mass spectroscopic characteristics of I#350. The peaks marked with a star

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are not protein identification specific but represents methodologically non-specific peaks.

Figure 8: Tryptic digestion mass spectroscopic characteristics of I#687. The peaks marked with a star are not protein identification specific but represents methodologically non-specific peaks.

Figure 9: Tryptic digestion mass spectroscopic characteristics of N#414. The peaks marked with a star are not protein identification specific but represents methodologically non-specific peaks.

Figure 10: Tryptic digestion mass spectroscopic characteristics of I#1035. The peaks marked with a star are not protein identification specific but represents methodologically non-specific peaks.

Figure 11: Tryptic digestion mass spectroscopic characteristics of N#26. The peaks marked with a star are not protein identification specific but represents methodologically non-specific peaks.

Figure 12: Tryptic digestion mass spectroscopic characteristics of N#31+N#32. The peaks marked with a star are not protein identification specific but represents methodologically non-specific peaks.

To identify proteins expressed at an increased level in differing endometrial conditions, endometrial samples were obtained as follows.

Normal menstrual cycle samples were obtained as described in Ref. 1. Endometrial biopsies were collected from 13 pre-menopausal, regular cycling women (35-50 years old) undergoing endometrial curettage (n=1) or hysterectomy (removal of the uterus) (n=12) for a variety of medical reasons not related to abnormality or malignancy of the endometrium. None used hormone contraception. For pathological condition samples, endometrial biopsies were collected from 16 patients (41 to 79 years old) undergoing endometrial curettage (n=9) or hysterectomy (n=7) for medical reasons related to abnormality or malignancy of the endometrium.

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The samples were treated as described in Ref. 1. The proteins of the endometrial biopsies were metabolically labelled with ^{35}S -methionine for 20 hours, and total cell lysates were processed for 2D gel electrophoresis, a technique in which proteins are separated in the first dimension according to the isoelectric point and in the second dimension according to the molecular weight. It was possible to study proteins with iso-electric points ranging from 3.5 to 11 and relative molecular weights ranging from 10 to 300 kDa. After electrophoresis the gels were fixed and treated for fluorography. The fluorograms of the 2D gel electrophoresis were subjected to quantitative analysis by computer-aided analysis, by which the density of each spot was quantified, the fluorogram patterns were matched i.e. numbers were assigned to each spot and the same spot was given the same number on all the fluorograms. The density (quantity synthesis) of each spot was assessed to find proteins with increased synthesis in endometrial adenocarcinoma or hyperplasia and assessed for periodic characteristics during the normal menstrual cycle to find proteins with the menstrual cycle-related synthesis.

Some of the menstrual cycle-related proteins so identified have been identified by amino acid sequence analysis (Ref.2). Selected menstrual cycle-related proteins were excised from several 2D gels, concentrated by 1D sodium dodecylsulphate polyacrylamide gel electrophoresis, and cleaved in situ by trypsin. The tryptic fragments were extracted and separated by reverse phase high pressure liquid chromatography. Finally, the partial amino-terminal amino acid sequence of selected tryptic fragments were determined for each protein. For identification the amino acid sequences of the tryptic fragments were compared to previously reported sequences by searching in databases.

The hyperplasia and adenocarcinoma associated proteins of the present invention may be sequenced and further characterised by similar methods.

Out of a total number of approximately 1,700 spots, 14 spots were found to have increased synthesis in hyperplasia.

The locations of these are shown in Figures 1 and 2. Some
5 27 spots had increased synthesis in adenocarcinoma. The locations of these are shown in Figures 3 and 4. The information obtained from the 2D-gel electrophoresis with respect to the isoelectric point (pI) and the molecular weight (MW) of the spots with increased synthesis in
10 hyperplasia is given in Table 1, and the spots with increased synthesis in adenocarcinoma are listed in Table 2.

Eight spots had increased expression in both hyperplasia and adenocarcinoma. Based on subjective evaluation, preferred subgroups of spots were selected with increased
15 synthesis in hyperplasia and in adenocarcinoma, respectively. The preferred subgroup of spots with increased synthesis in hyperplasia were selected as being the spots showing the highest relative increase in expression in hyperplasia as compared to the samples
20 obtained from women during the normal menstrual cycle and women with irregular proliferative phase endometrium. Similarly, the preferred subgroup of spots with increased synthesis in adenocarcinoma were selected as the spots showing the highest relative increase in expression in
25 adenocarcinoma as compared to the samples obtained from women during the normal menstrual cycle and women with irregular proliferative phase endometrium. The preferred subgroup of 7 spots with increased synthesis in hyperplasia is given in Table 3, and the preferred subgroup of 12 spots
30 with increased synthesis in adenocarcinoma is given in Table 4.

TABLE 1

Endometrial proteins with increased synthesis in hyperplasia		
Match #	pI	MW (kDa)
I#111	6.7	91
I#121	6.6	90
I#158	6.9	64
I#177	6.6	67
I#191	6.3	66
I#307	6.8	46
I#350	5.7	41
I#405	5.5	35
I#653	5.3	13
I#892	6.6	101
I#1183	5.8	14
N#126	7.4	51
N#148	8.2	44
N#414	9.5	48

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Table 2

Endometrial proteins with increased synthesis in adenocarcinoma		
Match #	pI	MW(kDa)
I#16	6.3	32
I#53	6.0	109
I#111	6.7	91
I#121	6.6	90
I#158	6.9	64
I#177	6.6	67
I#191	6.3	66
I#194	6.2	62
I#337	6.2	45
I#346	5.7	45
I#436	5.4	33
I#452	6.3	27
I#542	6.5	103
I#558	6.8	90
I#627	6.9	78
I#653	5.3	13
I#788	6.2	130
I#1137	6.3	66
I#1271	6.3	73
N#15	8.3	32
N#91	8.1	55
N#148	8.2	44
N#251	6.6	111
N#354	7.7	43
N#414	9.5	48
N#549	8.3	32
N#551	7.7	39

TABLE 3

Preferred endometrial proteins with increased synthesis in hyperplasia		
Match #	pI	MW(kDa)
I#111	6.7	91
I#158	6.9	64
I#191	6.3	66
I#350	5.7	41
I#405	5.5	35
I#653	5.3	13
I#892	6.6	101

5

TABLE 4

Preferred endometrial proteins with increased synthesis in adenocarcinoma		
Match #	pI	MW(kDa)
I#111	6.7	91
I#158	6.9	64
I#191	6.3	66
I#194	6.2	62
I#337	6.2	45
I#346	5.7	45
I#452	6.3	27
I#627	6.9	78
I#653	5.3	13
N#91	8.1	55
N#354	7.7	43
N#551	7.7	39

Out of the total number of approximately 1,700 spots, 135 had a menstrual cycle-related expression. These 135 spots had maximal expression as follows: 61 spots in proliferative endometrium, 29 spots in interval phase endometrium, 41 in secretory phase endometrium and 4 in late secretory/menstrual phase endometrium. The information obtained from the 2D-gel electrophoresis with respect to the isoelectric point (pI) and the molecular weight (MW) of a preferred subgroup of these spots which show increased synthesis in proliferative phase endometrium are given in Table 5 and their positions are indicated in Figures 5 and 6.

TABLE 5

Endometrial proteins with menstrual cycle-related expression Maximal expression in proliferative phase endometrium		
Match #	pI	MW(kDa)
I#103	6.9	86
I#590	5.4	34
I#687	5.6	67
I#960	5.3	23
I#1035	6.8	52
N#8	8.7	47
N#21	8.2	138
N#26	6.5	124
N#31	7.7	119
N#32	7.8	119
N#64	8.1	66
N#71	7.1	59
N#74	6.8	66
N#124	7.9	48
N#192	7.7	31
N#207	6.8	29
N#265	7.2	70
N#332	8.0	119
N#342	6.7	62

Fluorographs of gels exemplifying those upon which the
 5 identifications given in Tables 1 to 5 above are based
 appear in Figures 1 to 6.

The proteins described above may be further characterised by partial amino acid sequence analysis as described in Ref. 2, or by the more sensitive technique of mass spectrometric peptide mapping. By way of example, we have identified the proteins for which previously given names, data-base accession numbers and amino acid sequences are given in Table 6. Mass spectroscopic characteristics of tryptic digests of further proteins are shown in Figures 7 to 13 which have not matches to any known protein. These proteins can be sequenced by known techniques and are included per se within the scope of the invention.

15

TABLE 6

Match #	Name ID	Amino Acid Sequence
I#191 And I#1137 SEQ ID No.1	Human heat shock 70 kD protein 1 P08107	MAKAAAIGID LGTTYSCVGV FQHGKVEIIA NDQGNRTTPS YVAFDTERL IGDAAKNQVA LNPQNTVFDA KRLIGRKFGD PVVQSDMKHW PFQVINDGDK PKVQVSYKGE TKAFYPEEIS SMVLTKMKEI AEAYLGYPVT NAVITVPAYF NDSQRQATKD AGVIAGLNVL RIINEPTAAA IAYGLDRTGK GERNVLIFDL GGGTFDVSIL TIDDGIFEVK ATAGDTHLGG EDFDNRLVNH FVEEFKRKHK KDISQNKRAV RRLRTACERA KRTLSSSTQA SLEIDSLFEG IDFYTSITRA RFEELCSDLF RSTLEPVEKA LRDAKLDKAQ IHDVLVGGG TRIPKVQKLL QDFFNGRDLN KSINPDEAVA YGA AVQAAIL MGDKSENVQD LLLLDVAPLS LGLETAGGVM TALIKRNSTI PTKQTQIFTT YSDNQPGVLI QVYEGERAMT KDNLLGRFE LSGIPPAPRG VPQIEVTFDI DANGILNVTA TDKSTGKANK ITITNDKGRL SKEEIERMVQ EAEKYKAEDE VQRERVSAN ALESYAFNMK SAVEDEGLKG KISEADKKKV LDKCQEVISW LDANTLAEKD EFEHKRKELE QVCNPIISGL YQGAGGPGPG GFGAQGPKGG SGSGPTIEEV D
I#337 SEQ ID No.2	CAMP-dependent protein kinase type I-beta regulatory chain	ASPPACPSEE DESLKGCELY VQLHGIQQVL KDCIVHLCIS KPERPMKFLR EHFEEKLEKEE NRQILARQKS NSQSDSHDEE VSPTPPNPVV KARRRRGGVS AEVYTEEDAV SYVRKVIPKD YKMTALAKA ISKNVLF AHL DDNERSDIFD AMFPVTHIAG ETVIQQGNEG DNFYVVDQGE VDVYVNGEWV TNISEGGSFG ELALIYGTPR AATVKAKTDL KLWIDRDSY RRILMGSTLR

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	P31321	KRKMYYEEFLS KVSILESLEK WERLTVADRL EPVQFEDGEK IVVQGEPPGD FYIITEGTAS VLQRRSPNEE YVEVGRLGPS DYFGEIALLL NRPRAA TVVA RGPLKCVKLD RPRFERVLGP CSEILKRNIQ RYNSFISLTV
I#346 And I#405 SEQ ID No. 3	Vimentin P08670	STRSVSSSSY RRMFGGPGTA SRPSSSRSYV TTSTRYTSLG SALRPSTSR LYASSPGGVY ATRSSAVRLR SSVPGVRLQ DSVDFSLADA INTEFKNTRT NEKVELQELN DRFANYIDKV RFLEQQNKIL LAELEQLKGQ GKSRLGDLYE EEMRELRRQV DQLTNDKARV EVERDNLAED IMRLREKLQE EMLQREEAEN TLQSFRQDQD NASLARLDLE RKVESLQEEI AFLKKLHEEE IQELQAQIQE QHVQIDVDVS KPDLTAAALRD VRQQYESVAA KNLQEAEEWY KSKFADLSEA ANRNNDALRQ AKQESTEYRR QVQSLTCEVD ALKGTNESLE RQMREMEENF AVEAANYQDT IGRLQDEIQN MKEEMARHLR EYQDLLNVKM ALDIEIATYR KLEGEESRI SLPLPNFSSL NLRETNLDSL PLVDTHSKRT FLIKTVETRD GOVINETSQH HDDLE
I#452 SEQ ID No. 4	Heat Shock 27 KD Protein P04792 And Prohibitin P35232 (in admixture)	MTERRVPFSL LRGPSWDPFR DWYPHSRLFD QAFGLPRLPE EWSQWLGGSS WPGYVRPLPP AAIESPAVAA PAYSRALSRO LSSGVSEIRH TADRWRVSLD VNHFAPELDT VKTKDGVVEI TGKHEERQDE HGYISRCFTR KYTLPPGVDP TQVSSSLSPG GTLTVEAPMP KLATQSNEIT IPVTFESRAQ LGGRSCKIR MAAKVFESIG KFGALAVAG GVNNSALYNV DAGHRAVIFD RFRGVQDIVV GEGTHFLIPW VQKPIIFDCR SRPRNVPVIT GSKDLQNVNI TLRILFRPVA SQLPRIFTSI GEDYDERVLP SITTEILKSV VARFDAGELI TQRELVSQV SDDLTERAAT FGLILDVSL THLTFGKEFT EAVEAKQVAQ QEAERARFV EKAQQKKAA IISAEGDSKA AELIANSLAT AGDGLIELRK LEAAEDIAYQ LSRSRNITYL PAGQSVLLQL PQ
I#436 And I#590 SEQ ID No. 5	Tropomyosin fibroblast isoform TM3 P09494	MDAIKKKMQM LKLDKENALD RAEQAEADKK AAEDRSKQLE DELVSLQKKL KGTEDELQY SEALKDAQEK LELAEEKATD AEADVASLNR RIQLVEEELD RAQERLATAL QKLEEAEEKAA DESERGMKVI ESRAQKDEEK MEIQEIQLKE AKHIAEDADR KYEEVARKLV IIESDLERA ERAELSEGOV RQLEEQLRIM DQTLKALMAA EDKYSQKEDR YEEEIKVLSD KLKEAETRAE FAERSVTKE KSIDDLEEKV AHAKENLSM HQMLDQTLLE LNNM
I#627 SEQ ID No. 6	Serotrans- ferrin precursor P02787	MRLAVGALLV CAVLGLCLAV PDKTVRWCAV SEHEATKCQS FRDHMKSVIP SDGPSVACVK KASYLDCIRA IAANEADAVT LDAGLVYDAY LAPNNLKPVV AEFYGSKEDEP QTFYYAVAVV KKDSGFQMNQ LRGKKSCHTG LGRSAGWNIP IGLLYCDLPE PRKPLEKAVA NFFSGSCAPC ADGTDFFPQLC QLCPGCGCST LNQYFGYSGA FKCLKDGAGD VAFVKHSTIF ENLANKADRD QYELLCLDNT RKPVDEYKDC HLAQVPSHTV VARSMGGKED LIWELLNQAQ EHF GKDKSKE

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		FQLFSSPHGK DLLFKDSAAG FLKVPPRMDA KMYLGYEYVT AIRNLREGTC PEAPTDECKP VKWCALSHHE RLKCDDESVN SVGKIECVSA ETTEDCIAKI MNGEADAMSL DGGFVYIAGK CGLVPVLAEN YNKSNDNEDT PEAGYFAVAV VKKSASDLTW DNLKGKKSCH TAVGRTAGWN IPMGLLYNKI NHCRFDEFFS EGCAPGSKKD SSLCKLCMGS GLNLCEPNNK EGYGYTGAF RCLVEKGDVA FVKHQTVQPON TGGKNPDPA KNLNEKDYEL LCLDGTRKPV EYANCHLAR APNHAVVTRK DKEACVHKIL RQQQHLFGSN VTDCSGNFCL FRSETKDLLF RDDTVCLAKL HDRNTYEKYL GEEYVKAVGN LRKSTSSLL EACTFRRP
N#8 SEQ ID No.7	47 KD Heat Shock Protein Precursor P29043	MRSLLLGTLC LLAVALAAEV KKPVEAAAPG TAEKLSSKAT TLAEPSTGLA FSLYQAMAKD QAVENILVSP VVVASSLGLV SLGGKATTAS QAKAVLSAEQ LRDEEVHAGL GELLRSLSNS TARNVTWKLK SRLYGPSSVS FADDFVRSSK QHYNCEHSKI NFPDKRSALQ SINEWAAOTT DGKLPEVTKD VERTDGALLV NAMFFKPHWD EKFHKKMVDN RGFMTVRSYT VGVMTMHRTG LYNYYDDEKE KLQLVEMPLA HKLSSLIILM PHHVEPLERL EKLLTKEQLK IWMGKMOKKA VAISLPKGVV EVTHDLQKHL AGLGLTEAID KNKADLSRMS GKKDLYLASV FHATAFELDT DGNPFDQDIY GREELRSPKL FYADHPFIFL VRDTQSGSLL FIGRLVRLKG DKMRDEL
N#124 SEQ ID No.8	Ubiquinol- cytochrom C reductase complex core protein 2 precursor P22695	MKLLTRAGSF SRFYSLKVAP KVKATAAPAG APPQPQDLEF TKLPNGLVIA SLENYSPVSR IGLFIKAGSR YEDFSNLGTT HLLRLTSSLT TKGASSFKIT RGIEAVGGKL SVTATRENMA YTVECLRGDV DILMEFLNV TTAPEFRRWE VADLQPQLKI DKAVAFQNPQ THVIENLHAA AYQNALANPL YCPDYRIGKV TSEELHYFVQ NHFTSARMAL IGLGVSHPV LKQVAEQFLNM RGGLGLSGAK ANYRGGEIRE QNGDSLVAHA FVAESAVAGS AEANAFSVLQ HVLGAGPHVK RGSNTTSHLH QAVAKATQQP FVSAFNASY SDSGLFGIYT ISQATAAGDV IKAAYNQVKR IAQGNLSNTD VQAANKLKA GYLMSVESSE CFLEEVGSQA LVAGSYMPPS TVLQQIDSV NADIINAACK FVSGQKSMAA SGNLGHTPFV DEL
N#126 SEQ ID No.9	Alpha Enolase P06733	SILKIHAREI FDSRGNPTE VDLFTSKGLF RAAVPSGAST GIYEALRLD NDKTRYMGKG VSKAVEHINK TIAPALVSKK LNVTEQEKID KLMIEMDGTE NKSFGANAI LGVSLAVCKA GAVEKGVPLY RHIADLAGNS EVILPVPFAN VINGGSHAGN KLAMQEFMIL PVGAANFREA MRIGAEVYHN LKNVIKEYG KDATNVGDEG GFAPNILENK EGGLELKTAI GKAGYTDKVV IGMVAAASEF FRSGKYDLDF KSPDDPSRYI SPDQLADLYK SFIKDYPVVS IEDPFDQDDW GAWQKFTASA GIQVVGDDLT VTNPKRIAKA VNEKSCNCLL LKVNQIGSVT ESLQACKLAQ ANGWGMVSH RSGETEDTFI ADLVVGLCTG QIKTGAPCRS ERLAKYNQLL RIEEELGSKA KFAGRNFRNP LAK

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N#148 SEQ ID No.10	Phospho- glycerate kinase 1 P00558	SLSNKLTLDK LDVKGKRVVM RVDFNVPMKNNQITNNQRIK AAVPSIKFCL DNGAKSVVLM SHLGRPDGVP MPDKYSLEPV AVELKSLLGK DVLFLKDCVG PEVEKACANP AAGSVILLEN LRFHVEEEGK GKDASGNKVK AEPKIEAFR ASLSKLGDVY VNDAFGTAHR AHSSMVGVNL PQKAGGFLMK KELNYFAKAL ESPERPFLAI LGGAKVADKI QLINNMLDKV NEMIIGGGMA FTFLKVLNNM EIGTSLFDEE GAKIVKDLMS KAEKNGVKIT LPVDFVTADK FDENAKTGQA TVASGIPAGW MGLDCGPRESS KKYAEAVTRA KQIVWNGPVG VFEWEAFARG TKALMDEVVK ATSRGCITII GGGDTATCCA KWNTEDKVSH VSTGGGASLE LLEGKVLPGV DALSNIL
N#207 SEQ ID No.11	Triose- phosphat isomerase ISHUT S29743	MAPSRKFFVG GNWKMNGRKQ SLGELIGTLN AAKVPADTEV VCAPPTAYID FARQKLDPKI AVAAQNCYKV TNGAFTGEIS PGMKDCGAT WVVLGHSERR HVFGESDELI GQKVAHALAE GLGVIACIGE KLDEREAGIT EKVVEQTKV IADNVKDWSK VVLAYEPVWA IGTGKTATPQ QAQEVHEKLR GWLKSNSVDA VAQSTRIIYG GSVTGATCKE LASQPDVDGF LVGGASLKPE FVDIINAKQ
N#332 SEQ ID No.12	Hypo-thetical Protein KIAA0083 P51530	PVPLSFLSTV CDPVQDGAA ERTGAADGEE FLGGGGLPAE LFQKKVASF PRTVLSTGMD NRYLVLAVNT VQNKEGNCEK RLVITASQSL ENKELCILRN DWCSVPVEPG DIIHLEGDCT SDTWIIDKDF GYLILYPDML ISGTSIASSI RCMRRRAVLSE TFRSSDPATR QMLIGTVLHE VFQKAINNSF APEKLQELAF QTIQEIRHLK EMYRLNLSQD EIKQEVEDYL PSFCKWAGDF MHKNTSTDFF QMQLSLPSDN SKDNSTCNIE VVKPMDIEES IWSPRFGLKG KIDVTVGVKI HRGYKTKYKI MPELKTGKE SNSIEHRSQV VLYTLLSQER RADPEAGLLL YLKTGQMYPV PANHLDKREL LKLRNQMAFS LFHRISKSAT RQKTQLASLP QIEEEKTCK YCSQIGNCAL YSRAVEQQMD CSSVPIVMLP KIEEETQHLK QTHLEYFSLW CLMLTLESQS KDNKKNHQNI WLMPASEMEK SGSCIGNLIR MEHVKIVCDG QYLHNFQCKH GAIPVTNLMA GDRVIVSGEE RSLFALSRYG VKEINMTTVT CLLDRNLSVL PESTLFRDQ EEKNCDIDTP LGNLSKLMEN TFVSKKLRLD IIDFREPOFI SYLSSVLPHD AKDTVACILK GLNKPORQAM KKVLLSKDYT LIVGMPGTGK TTTICTLVRI LYACGFSVLL TSYTHSAVDN ILLKLAKFKI GFLRLGQIQK VHPAIQQFTE QEICRSKSIK SLALLEELYN SQLIVATTCM GINHPIFSRK IFDFCIVDEA SQISQPICLG PLFFSRRFVL VGDHQQLPPL VLNREARALG MSELFKRLE QNKSAVVOLT VQYRMNSKIM SLSNKLTYEG KLECGSDKVA NAVINLRHFK DVKLELEFYA OYSDNPWLMG VFEPNNPVCF LNTDKVPAPE QVEKGGVSNV TEAKLIVFLT SIFVKAGCSP SDIGIIAPYR QQLKIINDLL ARSIGMVEVN TVDKYQGRDK SIVLVSFVRS NKDGTVGELL KDWRRLNVAI TRAKHKLILL GCVPSLNCYP PLEKLLNHLN

		SEKLIIDLPS REHESLCHIL GDFQRE
N#342 SEQ ID No.13	Catalase P04040	MADSRDPASD QMQHWKEQRA AQKADVLTTG AGNPVGDKLN VITVGPRGPL LVQDVVFTDE MAHFDREIRIP ERVVHAKGAG AFGYFEVTHD ITKYSKAKVF EHIGKKTPIA VRFSTVAGES GSADTVRDPGR GFAVKFYTED GNWDLVGNNT PIFFIRDPIIL FPSFIHSQKR NPQTHLKOPD MVWDFWSLRP ESLHQVSFLF SDRGIPDGHR HMNGYGSHTF KLVNANGEAV YCKFHYKTDQ GIKNLSVEDA ARLSQEDPDY GIRDLFNAIA TGKYPSTWTFY IQVMTFNQAE TFPFNPFDLT KVWPHKDYPL IPVGKLVNLR NPVNYFAEVE QIAFDPSNMP PGIEASPDKM LQGRLEFAYPD THRHRLGPNY LHIPVNCPYR ARVANYQRDG PMCMQDNQGG APNYYPSNFG APEQQPSALE HSIQYSGEVR RFNTANDDNV TQVRAFVNVV LNEEQRKRLC ENIAGHLKDA QIFIQKKAVK NFEVHPDYG SHIQALLDKY NAEKPKNAIH TFVQSGSHLA AREKANL
N#551 SEQ ID No.14	Hetero- geneous nuclear ribonucleo- proteins A2/B1 P22626	MEKTLETVPL ERKKREKEQF RKLFIGGLSF ETTEESLRNY YEQWGLTDC VVMRDPASKR SRGFGFVTF SMAEVDAAAMA ARPHSIDGRV VEPKRAVARE ESGKPGAHTV VKKLFGVGGIK EDTEEHHLRD YFEEYGKIDT IEIITDRQSG KKRGFGFVTF DDHDPVDKIV LQKYHTINGH NAEVRKALSR QEMQEVQSSR SGRGGNFGFG DSRGGGGNFG PGPGSNFRGG SDGYGSGRGF GDYNGYGGG PGGGNFGGSP GYGGGRGGYG GGGPGYGNQG GYGGGGYDNY GGGNYGSGNY NDFGNYNQPF SNYGPMSGN FGGSRNMGGP YGGGNYGPGG SGGSGGYGGR SRY
I#960 (Prolifer ative phase marker) SEQ ID No.15	Steroid membrane binding protein X99714	MAAEDVAATG ADPSELEGGG LLHEIFTSPL NLLLLGLCIF LLYKIVRGDQ PAASDSDDE PPPLRLKRR DFTPAELRRF DGVQDPRILM AINGKVFVDT KGRKFYGPGE PYGVFAGRDA SRGLATFCLD KEALKDEYDD LSDLTPAQQE LNDWDWSQFT FKYHHVGKLL KEGEETPVYS DEEPPKDESA RKND
I#177 (Hyperpla sia & Cancer Marker) SEQ ID No.16	Heat shock cognate 71 KD protein P11142	MSKGPVAVGID LGTTYSCVGV FQHGKVEIIA NDQGNRTTPS YVAFTDTERL IGDAAKNQVA MNPTNTVFDA KRLIGRRFDD AVVQSDMKHW PFMVVNDAGR PKVQVEYKGE TKSFYPEEVS SMVLTKMKEI AEAYLGKTVT NAVVTVPAYF NDSQRQATKD AGTIAGLNVL RIINEPTAAA IAYGLDKKVG AERNVLIFDL GGGTDFVSIL TIEDGIFEVK STAGDTHLGG EDFDNRMVNH FIAEFKRKHK KDISENKRAV RRLRTACERA KRTLSSSTQA SIEIDSLYEG IDFYTSITRA RFEELNADLF RGTLDPVEKA LRDAKLKDSQ IHDIVLVGGS TRIPKIQKLL QDFFNGKELN KSINPDEAVA YGAAVQAAIL SGDKSENVQD LLLLDVTPLS LGIETAGGVM TVLIKRNTTI PTKQTQFTT YSDNQPGVLI QVYEGERAMT KDNLLGKFE LTGIPPAPRG VPQIEVTFDI DANGILNVSA VDKSTGKENK ITITNDKGRL SKEDIERMVQ EAEKYKAED KORDKVSSKN SLESYAFNMK ATVEDEKLQG KINDEDKQKI LDKCNEIINW LDKNQTAKE EFEHQQKELE KVCNPIITKL YQSAGMPPG MPGGFPGGGA PPSGGASSGP TIEEVD

ID: Accession Identification in protein or nucleotide databases
(e.g. SwissProt, Protein Identification Resource (PIR) or EMBL)

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The proteins of interest may be isolated from endometrial tissue or other protein sources by 2D gel electrophoresis or by using chromatographic techniques. Poly- or
5 monoclonal antibodies towards the protein of interest can be raised, and immunoassays can be established based on such antibodies. Synthetic peptides being fragments characteristic of such proteins may be used for the same purposes. Assays may be based on more than one such protein
10 for measurement at one time.

- Ref.1 : Byrjalsen et al. Hum Reprod 1995;10:13-18.
Ref.2 : Byrjalsen et al., Hum Reprod 1995;10:2760-2766.
Ref.3 : Julkunen et al., Endocrinology 1986;118:1782-1786.
15 Ref.4 : Byrjalsen et al., Obstet Gynecol 1992;79:523-528.
Ref.5 : Byrjalsen et al., Hum Reprod 1992;7:1042-1047.

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SEQUENCE LISTING

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(1) GENERAL INFORMATION:

10

(i) APPLICANT:

(A) NAME: Center for Clinical and Basic Research

15

(B) STREET: Ballerup Byvej 222,

(C) CITY: Ballerup

(E) COUNTRY: Denmark

(F) POSTAL CODE (ZIP): DK-2750

20

(ii) TITLE OF INVENTION: Biochemical Markers for the Human Endometrium

(iii) NUMBER OF SEQUENCES: 16

25

(iv) COMPUTER READABLE FORM:

(A) MEDIUM TYPE: Floppy disk

(B) COMPUTER: IBM PC compatible

(C) OPERATING SYSTEM: PC-DOS/MS-DOS

30

(D) SOFTWARE: PatentIn Release #1.0, Version #1.30 (EPO)

(vi) PRIOR APPLICATION DATA:

(A) APPLICATION NUMBER: GB 9618600.2

(B) FILING DATE: 06-SEP-1996

35

(vi) PRIOR APPLICATION DATA:

(A) APPLICATION NUMBER: GB 9707132.8

(B) FILING DATE: 08-APR-1997

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(2) INFORMATION FOR SEQ ID NO: 1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 641 amino acids

45

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

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(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

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(A) ORGANISM: homo sapiens

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

60

Met Ala Lys Ala Ala Ala Ile Gly Ile Asp Leu Gly Thr Thr Tyr Ser
1 5 10 15

65

Cys Val Gly Val Phe Gln His Gly Lys Val Glu Ile Ile Ala Asn Asp
20 25 30Gln Gly Asn Arg Thr Thr Pro Ser Tyr Val Ala Phe Thr Asp Thr Glu
35 40 45

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Arg Leu Ile Gly Asp Ala Ala Lys Asn Gln Val Ala Leu Asn Pro Gln
 50 55 60
 5 Asn Thr Val Phe Asp Ala Lys Arg Leu Ile Gly Arg Lys Phe Gly Asp
 65 70 75 80
 10 Pro Val Val Gln Ser Asp Met Lys His Trp Pro Phe Gln Val Ile Asn
 85 90 95
 15 Asp Gly Asp Lys Pro Lys Val Gln Val Ser Tyr Lys Gly Glu Thr Lys
 100 105 110
 20 Ala Phe Tyr Pro Glu Glu Ile Ser Ser Met Val Leu Thr Lys Met Lys
 115 120 125
 Glu Ile Ala Glu Ala Tyr Leu Gly Tyr Pro Val Thr Asn Ala Val Ile
 130 135 140
 25 Thr Val Pro Ala Tyr Phe Asn Asp Ser Gln Arg Gln Ala Thr Lys Asp
 145 150 155 160
 Ala Gly Val Ile Ala Gly Leu Asn Val Leu Arg Ile Ile Asn Glu Pro
 165 170 175
 30 Thr Ala Ala Ala Ile Ala Tyr Gly Leu Asp Arg Thr Gly Lys Gly Glu
 180 185 190
 35 Arg Asn Val Leu Ile Phe Asp Leu Gly Gly Gly Thr Phe Asp Val Ser
 195 200 205
 Ile Leu Thr Ile Asp Asp Gly Ile Phe Glu Val Lys Ala Thr Ala Gly
 210 215 220
 40 Asp Thr His Leu Gly Gly Glu Asp Phe Asp Asn Arg Leu Val Asn His
 225 230 235 240
 Phe Val Glu Glu Phe Lys Arg Lys His Lys Lys Asp Ile Ser Gln Asn
 245 250 255
 45 Lys Arg Ala Val Arg Arg Leu Arg Thr Ala Cys Glu Arg Ala Lys Arg
 260 265 270
 50 Thr Leu Ser Ser Ser Thr Gln Ala Ser Leu Glu Ile Asp Ser Leu Phe
 275 280 285
 Glu Gly Ile Asp Phe Tyr Thr Ser Ile Thr Arg Ala Arg Phe Glu Glu
 290 295 300
 55 Leu Cys Ser Asp Leu Phe Arg Ser Thr Leu Glu Pro Val Glu Lys Ala
 305 310 315 320
 Leu Arg Asp Ala Lys Leu Asp Lys Ala Gln Ile His Asp Leu Val Leu
 325 330 335
 60 Val Gly Gly Ser Thr Arg Ile Pro Lys Val Gln Lys Leu Leu Gln Asp
 340 345 350
 65 Phe Phe Asn Gly Arg Asp Leu Asn Lys Ser Ile Asn Pro Asp Glu Ala
 355 360 365
 Val Ala Tyr Gly Ala Ala Val Gln Ala Ala Ile Leu Met Gly Asp Lys
 370 375 380

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Ser Glu Asn Val Gln Asp Leu Leu Leu Leu Asp Val Ala Pro Leu Ser
 385 390 395 400
 5 Leu Gly Leu Glu Thr Ala Gly Gly Val Met Thr Ala Leu Ile Lys Arg
 405 410 415
 Asn Ser Thr Ile Pro Thr Lys Gln Thr Gln Ile Phe Thr Thr Tyr Ser
 420 425 430
 10
 Asp Asn Gln Pro Gly Val Leu Ile Gln Val Tyr Glu Gly Glu Arg Ala
 435 440 445
 15 Met Thr Lys Asp Asn Asn Leu Leu Gly Arg Phe Glu Leu Ser Gly Ile
 450 455 460
 20 Pro Pro Ala Pro Arg Gly Val Pro Gln Ile Glu Val Thr Phe Asp Ile
 465 470 475 480
 25 Asp Ala Asn Gly Ile Leu Asn Val Thr Ala Thr Asp Lys Ser Thr Gly
 485 490 495
 Lys Ala Asn Lys Ile Thr Ile Thr Asn Asp Lys Gly Arg Leu Ser Lys
 500 505 510
 30 Glu Glu Ile Glu Arg Met Val Gln Glu Ala Glu Lys Tyr Lys Ala Glu
 515 520 525
 Asp Glu Val Gln Arg Glu Arg Val Ser Ala Lys Asn Ala Leu Glu Ser
 530 535 540
 35 Tyr Ala Phe Asn Met Lys Ser Ala Val Glu Asp Glu Gly Leu Lys Gly
 545 550 555 560
 40 Lys Ile Ser Glu Ala Asp Lys Lys Lys Val Leu Asp Lys Cys Gln Glu
 565 570 575
 Val Ile Ser Trp Leu Asp Ala Asn Thr Leu Ala Glu Lys Asp Glu Phe
 580 585 590
 45 Glu His Lys Arg Lys Glu Leu Glu Gln Val Cys Asn Pro Ile Ile Ser
 595 600 605
 Gly Leu Tyr Gln Gly Ala Gly Gly Pro Gly Pro Gly Gly Phe Gly Ala
 610 615 620
 50 Gln Gly Pro Lys Gly Gly Ser Gly Ser Gly Pro Thr Ile Glu Glu Val
 625 630 635 640
 55 Asp

(2) INFORMATION FOR SEQ ID NO: 2:

- 60 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 380 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 65 (ii) MOLECULE TYPE: protein
 (iii) HYPOTHETICAL: NO

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(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: homo sapiens

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

10 Ala Ser Pro Pro Ala Cys Pro Ser Glu Glu Asp Glu Ser Leu Lys Gly
 1 5 10 15
 15 Cys Glu Leu Tyr Val Gln Leu His Gly Ile Gln Gln Val Leu Lys Asp
 20 25 30
 Cys Ile Val His Leu Cys Ile Ser Lys Pro Glu Arg Pro Met Lys Phe
 35 40 45
 20 Leu Arg Glu His Phe Glu Lys Leu Glu Lys Glu Glu Asn Arg Gln Ile
 50 55 60
 25 Leu Ala Arg Gln Lys Ser Asn Ser Gln Ser Asp Ser His Asp Glu Glu
 65 70 75 80
 Val Ser Pro Thr Pro Pro Asn Pro Val Val Lys Ala Arg Arg Arg Arg
 85 90 95
 30 Gly Gly Val Ser Ala Glu Val Tyr Thr Glu Glu Asp Ala Val Ser Tyr
 100 105 110
 Val Arg Lys Val Ile Pro Lys Asp Tyr Lys Thr Met Thr Ala Leu Ala
 115 120 125
 35 Lys Ala Ile Ser Lys Asn Val Leu Phe Ala His Leu Asp Asp Asn Glu
 130 135 140
 40 Arg Ser Asp Ile Phe Asp Ala Met Phe Pro Val Thr His Ile Ala Gly
 145 150 155 160
 Glu Thr Val Ile Gln Gln Gly Asn Glu Gly Asp Asn Phe Tyr Val Val
 165 170 175
 45 Asp Gln Gly Glu Val Asp Val Tyr Val Asn Gly Glu Trp Val Thr Asn
 180 185 190
 Ile Ser Glu Gly Gly Ser Phe Gly Glu Leu Ala Leu Ile Tyr Gly Thr
 195 200 205
 50 Pro Arg Ala Ala Thr Val Lys Ala Lys Thr Asp Leu Lys Leu Trp Gly
 210 215 220
 55 Ile Asp Arg Asp Ser Tyr Arg Arg Ile Leu Met Gly Ser Thr Leu Arg
 225 230 235 240
 Lys Arg Lys Met Tyr Glu Glu Phe Leu Ser Lys Val Ser Ile Leu Glu
 245 250 255
 60 Ser Leu Glu Lys Trp Glu Arg Leu Thr Val Ala Asp Arg Leu Glu Pro
 260 265 270
 Val Gln Phe Glu Asp Gly Glu Lys Ile Val Val Gln Gly Glu Pro Gly
 275 280 285
 65 Asp Asp Phe Tyr Ile Ile Thr Glu Gly Thr Ala Ser Val Leu Gln Arg
 290 295 300

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Arg Ser Pro Asn Glu Glu Tyr Val Glu Val Gly Arg Leu Gly Pro Ser
 305 310 315 320
 5 Asp Tyr Phe Gly Glu Ile Ala Leu Leu Leu Asn Arg Pro Arg Ala Ala
 325 330 335
 Thr Val Val Ala Arg Gly Pro Leu Lys Cys Val Lys Leu Asp Arg Pro
 340 345 350
 10 Arg Phe Glu Arg Val Leu Gly Pro Cys Ser Glu Ile Leu Lys Arg Asn
 355 360 365
 15 Ile Gln Arg Tyr Asn Ser Phe Ile Ser Leu Thr Val
 370 375 380

(2) INFORMATION FOR SEQ ID NO: 3:

20 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 465 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 25 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
 (A) ORGANISM: homo sapiens

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

40 Ser Thr Arg Ser Val Ser Ser Ser Ser Tyr Arg Arg Met Phe Gly Gly
 1 5 10 15
 Pro Gly Thr Ala Ser Arg Pro Ser Ser Ser Arg Ser Tyr Val Thr Thr
 20 25 30
 45 Ser Thr Arg Thr Tyr Ser Leu Gly Ser Ala Leu Arg Pro Ser Thr Ser
 35 40 45
 50 Arg Ser Leu Tyr Ala Ser Ser Pro Gly Gly Val Tyr Ala Thr Arg Ser
 50 55 60
 Ser Ala Val Arg Leu Arg Ser Ser Val Pro Gly Val Arg Leu Leu Gln
 65 70 75 80
 55 Asp Ser Val Asp Phe Ser Leu Ala Asp Ala Ile Asn Thr Glu Phe Lys
 85 90 95
 Asn Thr Arg Thr Asn Glu Lys Val Glu Leu Gln Glu Leu Asn Asp Arg
 100 105 110
 60 Phe Ala Asn Tyr Ile Asp Lys Val Arg Phe Leu Glu Gln Gln Asn Lys
 115 120 125
 65 Ile Leu Leu Ala Glu Leu Glu Gln Leu Lys Gly Gln Gly Lys Ser Arg
 130 135 140

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	Leu Gly Asp Leu Tyr Glu Glu Glu Met Arg Glu Leu Arg Arg Gln Val	145	150	155	160
5	Asp Gln Leu Thr Asn Asp Lys Ala Arg Val Glu Val Glu Arg Asp Asn	165	170	175	
	Leu Ala Glu Asp Ile Met Arg Leu Arg Glu Lys Leu Gln Glu Met	180	185	190	
10	Leu Gln Arg Glu Glu Ala Glu Asn Thr Leu Gln Ser Phe Arg Gln Asp	195	200	205	
15	Val Asp Asn Ala Ser Leu Ala Arg Leu Asp Leu Glu Arg Lys Val Glu	210	215	220	
20	Ser Leu Gln Glu Glu Ile Ala Phe Leu Lys Lys Leu His Glu Glu Glu	225	230	235	240
	Ile Gln Glu Leu Gln Ala Gln Ile Gln Glu Gln His Val Gln Ile Asp	245	250	255	
25	Val Asp Val Ser Lys Pro Asp Leu Thr Ala Ala Leu Arg Asp Val Arg	260	265	270	
	Gln Gln Tyr Glu Ser Val Ala Ala Lys Asn Leu Gln Glu Ala Glu Glu	275	280	285	
30	Trp Tyr Lys Ser Lys Phe Ala Asp Leu Ser Glu Ala Ala Asn Arg Asn	290	295	300	
35	Asn Asp Ala Leu Arg Gln Ala Lys Gln Glu Ser Thr Glu Tyr Arg Arg	305	310	315	320
	Gln Val Gln Ser Leu Thr Cys Glu Val Asp Ala Leu Lys Gly Thr Asn	325	330	335	
40	Glu Ser Leu Glu Arg Gln Met Arg Glu Met Glu Glu Asn Phe Ala Val	340	345	350	
	Glu Ala Ala Asn Tyr Gln Asp Thr Ile Gly Arg Leu Gln Asp Glu Ile	355	360	365	
45	Gln Asn Met Lys Glu Glu Met Ala Arg His Leu Arg Glu Tyr Gln Asp	370	375	380	
50	Leu Leu Asn Val Lys Met Ala Leu Asp Ile Glu Ile Ala Thr Tyr Arg	385	390	395	400
	Lys Leu Leu Glu Gly Glu Glu Ser Arg Ile Ser Leu Pro Leu Pro Asn	405	410	415	
55	Phe Ser Ser Leu Asn Leu Arg Glu Thr Asn Leu Asp Ser Leu Pro Leu	420	425	430	
	Val Asp Thr His Ser Lys Arg Thr Phe Leu Ile Lys Thr Val Glu Thr	435	440	445	
60	Arg Asp Gly Gln Val Ile Asn Glu Thr Ser Gln His His Asp Asp Leu	450	455	460	
65	Glu	465			

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(2) INFORMATION FOR SEQ ID NO: 4:

5 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 471 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: protein
 (iii) HYPOTHETICAL: NO
 (iv) ANTI-SENSE: NO
 15 (vi) ORIGINAL SOURCE:
 (A) ORGANISM: homo sapiens

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

25 Met Thr Glu Arg Arg Val Pro Phe Ser Leu Leu Arg Gly Pro Ser Trp
 1 5 10 15
 Asp Pro Phe Arg Asp Trp Tyr Pro His Ser Arg Leu Phe Asp Gln Ala
 20 25 30
 30 Phe Gly Leu Pro Arg Leu Pro Glu Glu Trp Ser Gln Trp Leu Gly Gly
 35 40 45
 Ser Ser Trp Pro Gly Tyr Val Arg Pro Leu Pro Pro Ala Ala Ile Glu
 50 55 60
 35 Ser Pro Ala Val Ala Ala Pro Ala Tyr Ser Arg Ala Leu Ser Arg Gln
 65 70 75 80
 40 Leu Ser Ser Gly Val Ser Glu Ile Arg His Thr Ala Asp Arg Trp Arg
 85 90 95
 Val Ser Leu Asp Val Asn His Phe Ala Pro Asp Glu Leu Thr Val Lys
 100 105 110
 45 Thr Lys Asp Gly Val Val Glu Ile Thr Gly Lys His Glu Glu Arg Gln
 115 120 125
 Asp Glu His Gly Tyr Ile Ser Arg Cys Phe Thr Arg Lys Tyr Thr Leu
 130 135 140
 50 Pro Pro Gly Val Asp Pro Thr Gln Val Ser Ser Ser Leu Ser Pro Glu
 145 150 155 160
 55 Gly Thr Leu Thr Val Glu Ala Pro Met Pro Lys Leu Ala Thr Gln Ser
 165 170 175
 Asn Glu Ile Thr Ile Pro Val Thr Phe Glu Ser Arg Ala Gln Leu Gly
 180 185 190
 60 Gly Arg Ser Cys Lys Ile Arg Met Ala Ala Lys Val Phe Glu Ser Ile
 195 200 205
 65 Gly Lys Phe Gly Leu Ala Leu Ala Val Ala Gly Gly Val Val Asn Ser
 210 215 220

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Ala Leu Tyr Asn Val Asp Ala Gly His Arg Ala Val Ile Phe Asp Arg
 225 230 235 240
 5 Phe Arg Gly Val Gln Asp Ile Val Val Gly Glu Gly Thr His Phe Leu
 245 250 255
 Ile Pro Trp Val Gln Lys Pro Ile Ile Phe Asp Cys Arg Ser Arg Pro
 260 265 270
 10 Arg Asn Val Pro Val Ile Thr Gly Ser Lys Asp Leu Gln Asn Val Asn
 275 280 285
 Ile Thr Leu Arg Ile Leu Phe Arg Pro Val Ala Ser Gln Leu Pro Arg
 290 295 300
 15 Ile Phe Thr Ser Ile Gly Glu Asp Tyr Asp Glu Arg Val Leu Pro Ser
 305 310 315 320
 20 Ile Thr Thr Glu Ile Leu Lys Ser Val Val Ala Arg Phe Asp Ala Gly
 325 330 335
 Glu Leu Ile Thr Gln Arg Glu Leu Val Ser Arg Gln Val Ser Asp Asp
 340 345 350
 25 Leu Thr Glu Arg Ala Ala Thr Phe Gly Leu Ile Leu Asp Asp Val Ser
 355 360 365
 30 Leu Thr His Leu Thr Phe Gly Lys Glu Phe Thr Glu Ala Val Glu Ala
 370 375 380
 Lys Gln Val Ala Gln Gln Glu Ala Glu Arg Ala Arg Phe Val Val Glu
 385 390 395 400
 35 Lys Ala Glu Gln Gln Lys Lys Ala Ala Ile Ile Ser Ala Glu Gly Asp
 405 410 415
 Ser Lys Ala Ala Glu Leu Ile Ala Asn Ser Leu Ala Thr Ala Gly Asp
 420 425 430
 40 Gly Leu Ile Glu Leu Arg Lys Leu Glu Ala Ala Glu Asp Ile Ala Tyr
 435 440 445
 45 Gln Leu Ser Arg Ser Arg Asn Ile Thr Tyr Leu Pro Ala Gly Gln Ser
 450 455 460
 Val Leu Leu Gln Leu Pro Gln
 465 470

50

(2) INFORMATION FOR SEQ ID NO: 5:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 284 amino acids
 55 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 (ii) MOLECULE TYPE: protein
 60 (iii) HYPOTHETICAL: NO
 (iv) ANTI-SENSE: NO
 65 (vi) ORIGINAL SOURCE:
 (A) ORGANISM: homo sapiens

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

5 Met Asp Ala Ile Lys Lys Lys Met Gln Met Leu Lys Leu Asp Lys Glu
 1 5 10 15
 Asn Ala Leu Asp Arg Ala Glu Gln Ala Glu Ala Asp Lys Lys Ala Ala
 20 25 30
 10 Glu Asp Arg Ser Lys Gln Leu Glu Asp Glu Leu Val Ser Leu Gln Lys
 35 40 45
 Lys Leu Lys Gly Thr Glu Asp Glu Leu Asp Lys Tyr Ser Glu Ala Leu
 50 55 60
 15 Lys Asp Ala Gln Glu Lys Leu Glu Leu Ala Glu Lys Lys Ala Thr Asp
 65 70 75 80
 20 Ala Glu Ala Asp Val Ala Ser Leu Asn Arg Arg Ile Gln Leu Val Glu
 85 90 95
 Glu Glu Leu Asp Arg Ala Gln Glu Arg Leu Ala Thr Ala Leu Gln Lys
 100 105 110
 25
 Leu Glu Glu Ala Glu Lys Ala Ala Asp Glu Ser Glu Arg Gly Met Lys
 115 120 125
 30 Val Ile Glu Ser Arg Ala Gln Lys Asp Glu Glu Lys Met Glu Ile Gln
 130 135 140
 Glu Ile Gln Leu Lys Glu Ala Lys His Ile Ala Glu Asp Ala Asp Arg
 145 150 155 160
 35 Lys Tyr Glu Glu Val Ala Arg Lys Leu Val Ile Ile Glu Ser Asp Leu
 165 170 175
 40 Glu Arg Ala Glu Glu Arg Ala Glu Leu Ser Glu Gly Gln Val Arg Gln
 180 185 190
 Leu Glu Glu Gln Leu Arg Ile Met Asp Gln Thr Leu Lys Ala Leu Met
 195 200 205
 45 Ala Ala Glu Asp Lys Tyr Ser Gln Lys Glu Asp Arg Tyr Glu Glu Glu
 210 215 220
 Ile Lys Val Leu Ser Asp Lys Leu Lys Glu Ala Glu Thr Arg Ala Glu
 225 230 235 240
 50 Phe Ala Glu Arg Ser Val Thr Lys Leu Glu Lys Ser Ile Asp Asp Leu
 245 250 255
 55 Glu Glu Lys Val Ala His Ala Lys Glu Glu Asn Leu Ser Met His Gln
 260 265 270
 Met Leu Asp Gln Thr Leu Leu Glu Leu Asn Asn Met
 275 280

60

65

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(2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 698 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
 (A) ORGANISM: homo sapiens

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

Met Arg Leu Ala Val Gly Ala Leu Leu Val Cys Ala Val Leu Gly Leu
 1 5 10 15

Cys Leu Ala Val Pro Asp Lys Thr Val Arg Trp Cys Ala Val Ser Glu
 20 25 30

His Glu Ala Thr Lys Cys Gln Ser Phe Arg Asp His Met Lys Ser Val
 35 40 45

Ile Pro Ser Asp Gly Pro Ser Val Ala Cys Val Lys Lys Ala Ser Tyr
 50 55 60

Leu Asp Cys Ile Arg Ala Ile Ala Ala Asn Glu Ala Asp Ala Val Thr
 65 70 75 80

Leu Asp Ala Gly Leu Val Tyr Asp Ala Tyr Leu Ala Pro Asn Asn Leu
 85 90 95

Lys Pro Val Val Ala Glu Phe Tyr Gly Ser Lys Glu Asp Pro Gln Thr
 100 105 110

Phe Tyr Tyr Ala Val Ala Val Val Lys Lys Asp Ser Gly Phe Gln Met
 115 120 125

Asn Gln Leu Arg Gly Lys Lys Ser Cys His Thr Gly Leu Gly Arg Ser
 130 135 140

Ala Gly Trp Asn Ile Pro Ile Gly Leu Leu Tyr Cys Asp Leu Pro Glu
 145 150 155 160

Pro Arg Lys Pro Leu Glu Lys Ala Val Ala Asn Phe Phe Ser Gly Ser
 165 170 175

Cys Ala Pro Cys Ala Asp Gly Thr Asp Phe Pro Gln Leu Cys Gln Leu
 180 185 190

Cys Pro Gly Cys Gly Cys Ser Thr Leu Asn Gln Tyr Phe Gly Tyr Ser
 195 200 205

Gly Ala Phe Lys Cys Leu Lys Asp Gly Ala Gly Asp Val Ala Phe Val
 210 215 220

Lys His Ser Thr Ile Phe Glu Asn Leu Ala Asn Lys Ala Asp Arg Asp
 225 230 235 240

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	Gln Tyr Glu Leu Leu Cys Leu Asp Asn Thr Arg Lys Pro Val Asp Glu	
	245	250 255
5	Tyr Lys Asp Cys His Leu Ala Gln Val Pro Ser His Thr Val Val Ala	
	260	265 270
	Arg Ser Met Gly Gly Lys Glu Asp Leu Ile Trp Glu Leu Leu Asn Gln	
	275	280 285
10	Ala Gln Glu His Phe Gly Lys Asp Lys Ser Lys Glu Phe Gln Leu Phe	
	290	295 300
	Ser Ser Pro His Gly Lys Asp Leu Leu Phe Lys Asp Ser Ala His Gly	
	305	310 315 320
	Phe Leu Lys Val Pro Pro Arg Met Asp Ala Lys Met Tyr Leu Gly Tyr	
	325	330 335
20	Glu Tyr Val Thr Ala Ile Arg Asn Leu Arg Glu Gly Thr Cys Pro Glu	
	340	345 350
	Ala Pro Thr Asp Glu Cys Lys Pro Val Lys Trp Cys Ala Leu Ser His	
	355	360 365
25	His Glu Arg Leu Lys Cys Asp Glu Trp Ser Val Asn Ser Val Gly Lys	
	370	375 380
	Ile Glu Cys Val Ser Ala Glu Thr Thr Glu Asp Cys Ile Ala Lys Ile	
	385	390 395 400
30	Met Asn Gly Glu Ala Asp Ala Met Ser Leu Asp Gly Gly Phe Val Tyr	
	405	410 415
35	Ile Ala Gly Lys Cys Gly Leu Val Pro Val Leu Ala Glu Asn Tyr Asn	
	420	425 430
	Lys Ser Asp Asn Cys Glu Asp Thr Pro Glu Ala Gly Tyr Phe Ala Val	
	435	440 445
40	Ala Val Val Lys Lys Ser Ala Ser Asp Leu Thr Trp Asp Asn Leu Lys	
	450	455 460
	Gly Lys Lys Ser Cys His Thr Ala Val Gly Arg Thr Ala Gly Trp Asn	
	465	470 475 480
	Ile Pro Met Gly Leu Leu Tyr Asn Lys Ile Asn His Cys Arg Phe Asp	
	485	490 495
50	Glu Phe Phe Ser Glu Gly Cys Ala Pro Gly Ser Lys Lys Asp Ser Ser	
	500	505 510
	Leu Cys Lys Leu Cys Met Gly Ser Gly Leu Asn Leu Cys Glu Pro Asn	
	515	520 525
55	Asn Lys Glu Gly Tyr Tyr Gly Tyr Thr Gly Ala Phe Arg Cys Leu Val	
	530	535 540
60	Glu Lys Gly Asp Val Ala Phe Val Lys His Gln Thr Val Pro Gln Asn	
	545	550 555 560
	Thr Gly Gly Lys Asn Pro Asp Pro Trp Ala Lys Asn Leu Asn Glu Lys	
	565	570 575
65	Asp Tyr Glu Leu Leu Cys Leu Asp Gly Thr Arg Lys Pro Val Glu Glu	
	580	585 590

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Tyr Ala Asn Cys His Leu Ala Arg Ala Pro Asn His Ala Val Val Thr
 595 600 605
 5 Arg Lys Asp Lys Glu Ala Cys Val His Lys Ile Leu Arg Gln Gln Gln
 610 615 620
 His Leu Phe Gly Ser Asn Val Thr Asp Cys Ser Gly Asn Phe Cys Leu
 625 630 635 640
 10 Phe Arg Ser Glu Thr Lys Asp Leu Leu Phe Arg Asp Asp Thr Val Cys
 645 650 655
 Leu Ala Lys Leu His Asp Arg Asn Thr Tyr Glu Lys Tyr Leu Gly Glu
 660 665 670
 15 Glu Tyr Val Lys Ala Val Gly Asn Leu Arg Lys Cys Ser Thr Ser Ser
 675 680 685
 20 Leu Leu Glu Ala Cys Thr Phe Arg Arg Pro
 690 695

(2) INFORMATION FOR SEQ ID NO: 7:

25 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 417 amino acids
 (B) TYPE: amino acid
 30 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
 (A) ORGANISM: homo sapiens

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

45 Met Arg Ser Leu Leu Leu Gly Thr Leu Cys Leu Leu Ala Val Ala Leu
 1 5 10 15
 Ala Ala Glu Val Lys Lys Pro Val Glu Ala Ala Ala Pro Gly Thr Ala
 20 25 30
 50 Glu Lys Leu Ser Ser Lys Ala Thr Thr Leu Ala Glu Pro Ser Thr Gly
 35 40 45
 Leu Ala Phe Ser Leu Tyr Gln Ala Met Ala Lys Asp Gln Ala Val Glu
 50 55 60
 55 Asn Ile Leu Val Ser Pro Val Val Val Ala Ser Ser Leu Gly Leu Val
 65 70 75 80
 60 Ser Leu Gly Gly Lys Ala Thr Thr Ala Ser Gln Ala Lys Ala Val Leu
 85 90 95
 65 Ser Ala Glu Gln Leu Arg Asp Glu Glu Val His Ala Gly Leu Gly Glu
 100 105 110
 Leu Leu Arg Ser Leu Ser Asn Ser Thr Ala Arg Asn Val Thr Trp Lys
 115 120 125

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Leu Gly Ser Arg Leu Tyr Gly Pro Ser Ser Val Ser Phe Ala Asp Asp
 130 135 140
 5 Phe Val Arg Ser Ser Lys Gln His Tyr Asn Cys Glu His Ser Lys Ile
 145 150 155 160
 Asn Phe Pro Asp Lys Arg Ser Ala Leu Gln Ser Ile Asn Glu Trp Ala
 165 170 175
 10 Ala Gln Thr Thr Asp Gly Lys Leu Pro Glu Val Thr Lys Asp Val Glu
 180 185 190
 Arg Thr Asp Gly Ala Leu Leu Val Asn Ala Met Phe Phe Lys Pro His
 195 200 205
 15 Trp Asp Glu Lys Phe His His Lys Met Val Asp Asn Arg Gly Phe Met
 210 215 220
 20 Val Thr Arg Ser Tyr Thr Val Gly Val Thr Met Met His Arg Thr Gly
 225 230 235 240
 Leu Tyr Asn Tyr Tyr Asp Asp Glu Lys Glu Lys Leu Gln Leu Val Glu
 245 250 255
 25 Met Pro Leu Ala His Lys Leu Ser Ser Leu Ile Ile Leu Met Pro His
 260 265 270
 His Val Glu Pro Leu Glu Arg Leu Glu Lys Leu Leu Thr Lys Glu Gln
 275 280 285
 30 Leu Lys Ile Trp Met Gly Lys Met Gln Lys Lys Ala Val Ala Ile Ser
 290 295 300
 35 Leu Pro Lys Gly Val Val Glu Val Thr His Asp Leu Gln Lys His Leu
 305 310 315 320
 40 Ala Gly Leu Gly Leu Thr Glu Ala Ile Asp Lys Asn Lys Ala Asp Leu
 325 330 335
 Ser Arg Met Ser Gly Lys Lys Asp Leu Tyr Leu Ala Ser Val Phe His
 340 345 350
 45 Ala Thr Ala Phe Glu Leu Asp Thr Asp Gly Asn Pro Phe Asp Gln Asp
 355 360 365
 Ile Tyr Gly Arg Glu Glu Leu Arg Ser Pro Lys Leu Phe Tyr Ala Asp
 370 375 380
 50 His Pro Phe Ile Phe Leu Val Arg Asp Thr Gln Ser Gly Ser Leu Leu
 385 390 395 400
 Phe Ile Gly Arg Leu Val Arg Leu Lys Gly Asp Lys Met Arg Asp Glu
 405 410 415
 55 Leu

60 (2) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 453 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

65

(ii) MOLECULE TYPE: protein

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(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: homo sapiens

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

5 Met Lys Leu Leu Thr Arg Ala Gly Ser Phe Ser Arg Phe Tyr Ser Leu
 1 5 10 15
 15 Lys Val Ala Pro Lys Val Lys Ala Thr Ala Ala Pro Ala Gly Ala Pro
 20 20 25 30
 20 Pro Gln Pro Gln Asp Leu Glu Phe Thr Lys Leu Pro Asn Gly Leu Val
 35 40 45
 25 Ile Ala Ser Leu Glu Asn Tyr Ser Pro Val Ser Arg Ile Gly Leu Phe
 50 55 60
 25 Ile Lys Ala Gly Ser Arg Tyr Glu Asp Phe Ser Asn Leu Gly Thr Thr
 65 70 75 80
 30 His Leu Leu Arg Leu Thr Ser Ser Leu Thr Thr Lys Gly Ala Ser Ser
 85 90 95
 30 Phe Lys Ile Thr Arg Gly Ile Glu Ala Val Gly Gly Lys Leu Ser Val
 100 105 110
 35 Thr Ala Thr Arg Glu Asn Met Ala Tyr Thr Val Glu Cys Leu Arg Gly
 115 120 125
 40 Asp Val Asp Ile Leu Met Glu Phe Leu Leu Asn Val Thr Thr Ala Pro
 130 135 140
 Glu Phe Arg Arg Trp Glu Val Ala Asp Leu Gln Pro Gln Leu Lys Ile
 145 150 155 160
 45 Asp Lys Ala Val Ala Phe Gln Asn Pro Gln Thr His Val Ile Glu Asn
 165 170 175
 50 Leu His Ala Ala Ala Tyr Gln Asn Ala Leu Ala Asn Pro Leu Tyr Cys
 180 185 190
 50 Pro Asp Tyr Arg Ile Gly Lys Val Thr Ser Glu Glu Leu His Tyr Phe
 195 200 205
 55 Val Gln Asn His Phe Thr Ser Ala Arg Met Ala Leu Ile Gly Leu Gly
 210 215 220
 60 Val Ser His Pro Val Leu Lys Gln Val Ala Glu Gln Phe Leu Asn Met
 225 230 235 240
 60 Arg Gly Gly Leu Gly Leu Ser Gly Ala Lys Ala Asn Tyr Arg Gly Gly
 245 250 255
 65 Glu Ile Arg Glu Gln Asn Gly Asp Ser Leu Val His Ala Ala Phe Val
 260 265 270
 Ala Glu Ser Ala Val Ala Gly Ser Ala Glu Ala Asn Ala Phe Ser Val
 275 280 285

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Leu Gln His Val Leu Gly Ala Gly Pro His Val Lys Arg Gly Ser Asn
 290 295 300
 5 Thr Thr Ser His Leu His Gln Ala Val Ala Lys Ala Thr Gln Gln Pro
 305 310 315 320
 Phe Asp Val Ser Ala Phe Asn Ala Ser Tyr Ser Asp Ser Gly Leu Phe
 325 330 335
 10 Gly Ile Tyr Thr Ile Ser Gln Ala Thr Ala Ala Gly Asp Val Ile Lys
 340 345 350
 15 Ala Ala Tyr Asn Gln Val Lys Arg Ile Ala Gln Gly Asn Leu Ser Asn
 355 360 365
 Thr Asp Val Gln Ala Ala Lys Asn Lys Leu Lys Ala Gly Tyr Leu Met
 370 375 380
 20 Ser Val Glu Ser Ser Glu Cys Phe Leu Glu Glu Val Gly Ser Gln Ala
 385 390 395 400
 Leu Val Ala Gly Ser Tyr Met Pro Pro Ser Thr Val Leu Gln Gln Ile
 405 410 415
 25 Asp Ser Val Ala Asn Ala Asp Ile Ile Asn Ala Ala Lys Lys Phe Val
 420 425 430
 30 Ser Gly Gln Lys Ser Met Ala Ala Ser Gly Asn Leu Gly His Thr Pro
 435 440 445
 Phe Val Asp Glu Leu
 450

35 (2) INFORMATION FOR SEQ ID NO: 9:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 433 amino acids

40 (B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: NO

50 (iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: homo sapiens

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

Ser Ile Leu Lys Ile His Ala Arg Glu Ile Phe Asp Ser Arg Gly Asn
 1 5 10 15
 60 Pro Thr Val Glu Val Asp Leu Phe Thr Ser Lys Gly Leu Phe Arg Ala
 20 25 30
 Ala Val Pro Ser Gly Ala Ser Thr Gly Ile Tyr Glu Ala Leu Glu Leu
 35 40 45
 65 Arg Asp Asn Asp Lys Thr Arg Tyr Met Gly Lys Gly Val Ser Lys Ala
 50 55 60

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	Val	Glu	His	Ile	Asn	Lys	Thr	Ile	Ala	Pro	Ala	Leu	Val	Ser	Lys	Lys	65	70	75	80
5	Leu	Asn	Val	Thr	Glu	Gln	Glu	Lys	Ile	Asp	Lys	Leu	Met	Ile	Glu	Met	85	90	95	
	Asp	Gly	Thr	Glu	Asn	Lys	Ser	Lys	Phe	Gly	Ala	Asn	Ala	Ile	Leu	Gly	100	105	110	
10	Val	Ser	Leu	Ala	Val	Cys	Lys	Ala	Gly	Ala	Val	Glu	Lys	Gly	Val	Pro	115	120	125	
	Leu	Tyr	Arg	His	Ile	Ala	Asp	Leu	Ala	Gly	Asn	Ser	Glu	Val	Ile	Leu	130	135	140	
15	Pro	Val	Pro	Ala	Phe	Asn	Val	Ile	Asn	Gly	Gly	Ser	His	Ala	Gly	Asn	145	150	155	160
20	Lys	Leu	Ala	Met	Gln	Glu	Phe	Met	Ile	Leu	Pro	Val	Gly	Ala	Ala	Asn	165	170	175	
	Phe	Arg	Glu	Ala	Met	Arg	Ile	Gly	Ala	Glu	Val	Tyr	His	Asn	Leu	Lys	180	185	190	
25	Asn	Val	Ile	Lys	Glu	Lys	Tyr	Gly	Lys	Asp	Ala	Thr	Asn	Val	Gly	Asp	195	200	205	
30	Glu	Gly	Gly	Phe	Ala	Pro	Asn	Ile	Leu	Glu	Asn	Lys	Glu	Gly	Leu	Glu	210	215	220	
	Leu	Leu	Lys	Thr	Ala	Ile	Gly	Lys	Ala	Gly	Tyr	Thr	Asp	Lys	Val	Val	225	230	235	240
35	Ile	Gly	Met	Asp	Val	Ala	Ala	Ser	Glu	Phe	Phe	Arg	Ser	Gly	Lys	Tyr	245	250	255	
40	Asp	Leu	Asp	Phe	Lys	Ser	Pro	Asp	Asp	Pro	Ser	Arg	Tyr	Ile	Ser	Pro	260	265	270	
	Asp	Gln	Leu	Ala	Asp	Leu	Tyr	Lys	Ser	Phe	Ile	Lys	Asp	Tyr	Pro	Val	275	280	285	
45	Val	Ser	Ile	Glu	Asp	Pro	Phe	Asp	Gln	Asp	Asp	Trp	Gly	Ala	Trp	Gln	290	295	300	
50	Lys	Phe	Thr	Ala	Ser	Ala	Gly	Ile	Gln	Val	Val	Gly	Asp	Asp	Leu	Thr	305	310	315	320
	Val	Thr	Asn	Pro	Lys	Arg	Ile	Ala	Lys	Ala	Val	Asn	Glu	Lys	Ser	Cys	325	330	335	
55	Asn	Cys	Leu	Leu	Leu	Lys	Val	Asn	Gln	Ile	Gly	Ser	Val	Thr	Glu	Ser	340	345	350	
60	Leu	Gln	Ala	Cys	Lys	Leu	Ala	Gln	Ala	Asn	Gly	Trp	Gly	Val	Met	Val	355	360	365	
	Ser	His	Arg	Ser	Gly	Glu	Thr	Glu	Asp	Thr	Phe	Ile	Ala	Asp	Leu	Val	370	375	380	
65	Val	Gly	Leu	Cys	Thr	Gly	Gln	Ile	Lys	Thr	Gly	Ala	Pro	Cys	Arg	Ser	385	390	395	400
	Glu	Arg	Leu	Ala	Lys	Tyr	Asn	Gln	Leu	Leu	Arg	Ile	Glu	Glu	Glu	Leu	405	410	415	

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Gly Ser Lys Ala Lys Phe Ala Gly Arg Asn Phe Arg Asn Pro Leu Ala
 420 425 430

5

Lys

(2) INFORMATION FOR SEQ ID NO: 10:

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 417 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

15

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: NO

20

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(A) ORGANISM: homo sapiens

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:

30

Ser Leu Ser Asn Lys Leu Thr Leu Asp Lys Leu Asp Val Lys Gly Lys
 1 5 10 15

Arg Val Val Met Arg Val Asp Phe Asn Val Pro Met Lys Asn Asn Gln
 20 25 30

35

Ile Thr Asn Asn Gln Arg Ile Lys Ala Ala Val Pro Ser Ile Lys Phe
 35 40 45

40

Cys Leu Asp Asn Gly Ala Lys Ser Val Val Leu Met Ser His Leu Gly
 50 55 60

45

Arg Pro Asp Gly Val Pro Met Pro Asp Lys Tyr Ser Leu Glu Pro Val
 65 70 75 80

Ala Val Glu Leu Lys Ser Leu Leu Gly Lys Asp Val Leu Phe Leu Lys
 85 90 95

50

Asp Cys Val Gly Pro Glu Val Glu Lys Ala Cys Ala Asn Pro Ala Ala
 100 105 110

Gly Ser Val Ile Leu Leu Glu Asn Leu Arg Phe His Val Glu Glu Glu
 115 120 125

55

Gly Lys Gly Lys Asp Ala Ser Gly Asn Lys Val Lys Ala Glu Pro Ala
 130 135 140

60

Lys Ile Glu Ala Phe Arg Ala Ser Leu Ser Lys Leu Gly Asp Val Tyr
 145 150 155 160

Val Asn Asp Ala Phe Gly Thr Ala His Arg Ala His Ser Ser Met Val
 165 170 175

65

Gly Val Asn Leu Pro Gln Lys Ala Gly Gly Phe Leu Met Lys Lys Glu
 180 185 190

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Leu Asn Tyr Phe Ala Lys Ala Leu Glu Ser Pro Glu Arg Pro Phe Leu
 195 200 205
 5 Ala Ile Leu Gly Gly Ala Lys Val Ala Asp Lys Ile Gln Leu Ile Asn
 210 215 220
 Asn Met Leu Asp Lys Val Asn Glu Met Ile Ile Gly Gly Gly Met Ala
 225 230 235 240
 10 Phe Thr Phe Leu Lys Val Leu Asn Asn Met Glu Ile Gly Thr Ser Leu
 245 250 255
 Phe Asp Glu Glu Gly Ala Lys Ile Val Lys Asp Leu Met Ser Lys Ala
 15 260 265 270
 Glu Lys Asn Gly Val Lys Ile Thr Leu Pro Val Asp Phe Val Thr Ala
 275 280 285
 20 Asp Lys Phe Asp Glu Asn Ala Lys Thr Gly Gln Ala Thr Val Ala Ser
 290 295 300
 Gly Ile Pro Ala Gly Trp Met Gly Leu Asp Cys Gly Pro Glu Ser Ser
 25 305 310 315 320
 Lys Lys Tyr Ala Glu Ala Val Thr Arg Ala Lys Gln Ile Val Trp Asn
 325 330 335
 30 Gly Pro Val Gly Val Phe Glu Trp Glu Ala Phe Ala Arg Gly Thr Lys
 340 345 350
 Ala Leu Met Asp Glu Val Val Lys Ala Thr Ser Arg Gly Cys Ile Thr
 355 360 365
 35 Ile Ile Gly Gly Gly Asp Thr Ala Thr Cys Cys Ala Lys Trp Asn Thr
 370 375 380
 Glu Asp Lys Val Ser His Val Ser Thr Gly Gly Gly Ala Ser Leu Glu
 385 390 395 400
 40 Leu Leu Glu Gly Lys Val Leu Pro Gly Val Asp Ala Leu Ser Asn Ile
 405 410 415
 45 Leu

(2) INFORMATION FOR SEQ ID NO: 11:

- (i) SEQUENCE CHARACTERISTICS:
 50 (A) LENGTH: 249 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 55 (ii) MOLECULE TYPE: protein
 (iii) HYPOTHETICAL: NO
 60 (iv) ANTI-SENSE: NO
 (vi) ORIGINAL SOURCE:
 (A) ORGANISM: homo sapiens
 65 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:
 Met Ala Pro Ser Arg Lys Phe Phe Val Gly Gly Asn Trp Lys Met Asn
 1 5 10 15

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Gly Arg Lys Gln Ser Leu Gly Glu Leu Ile Gly Thr Leu Asn Ala Ala
 20 25 30
 5 Lys Val Pro Ala Asp Thr Glu Val Val Cys Ala Pro Pro Thr Ala Tyr
 35 40 45
 Ile Asp Phe Ala Arg Gln Lys Leu Asp Pro Lys Ile Ala Val Ala Ala
 50 55 60
 10 Gln Asn Cys Tyr Lys Val Thr Asn Gly Ala Phe Thr Gly Glu Ile Ser
 65 70 75 80
 Pro Gly Met Ile Lys Asp Cys Gly Ala Thr Trp Val Val Leu Gly His
 85 90 95
 Ser Glu Arg Arg His Val Phe Gly Glu Ser Asp Glu Leu Ile Gly Gln
 100 105 110
 20 Lys Val Ala His Ala Leu Ala Glu Gly Leu Gly Val Ile Ala Cys Ile
 115 120 125
 Gly Glu Lys Leu Asp Glu Arg Glu Ala Gly Ile Thr Glu Lys Val Val
 130 135 140
 25 Phe Glu Gln Thr Lys Val Ile Ala Asp Asn Val Lys Asp Trp Ser Lys
 145 150 155 160
 Val Val Leu Ala Tyr Glu Pro Val Trp Ala Ile Gly Thr Gly Lys Thr
 165 170 175
 30 Ala Thr Pro Gln Ala Gln Glu Val His Glu Lys Leu Arg Gly Trp
 180 185 190
 35 Leu Lys Ser Asn Val Ser Asp Ala Val Ala Gln Ser Thr Arg Ile Ile
 195 200 205
 Tyr Gly Gly Ser Val Thr Gly Ala Thr Cys Lys Glu Leu Ala Ser Gln
 210 215 220
 40 Pro Asp Val Asp Gly Phe Leu Val Gly Gly Ala Ser Leu Lys Pro Glu
 225 230 235 240
 45 Phe Val Asp Ile Ile Asn Ala Lys Gln
 245

(2) INFORMATION FOR SEQ ID NO: 12:

- 50 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 1076 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 55 (ii) MOLECULE TYPE: protein
 (iii) HYPOTHETICAL: NO
 60 (iv) ANTI-SENSE: NO
 (vi) ORIGINAL SOURCE:
 (A) ORGANISM: homo sapiens
 65

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

5	Pro	Val	Pro	Leu	Ser	Phe	Leu	Ser	Thr	Val	Cys	Asp	Pro	Arg	Val	Gln	1	5	10	15
	Asp	Gly	Ala	Ala	Glu	Arg	Thr	Gly	Ala	Ala	Asp	Gly	Glu	Glu	Phe	Leu	20	25	30	
10	Gly	Gly	Gly	Gly	Leu	Pro	Ala	Glu	Leu	Phe	Gln	Lys	Lys	Val	Val	Ala	35	40	45	
	Ser	Phe	Pro	Arg	Thr	Val	Leu	Ser	Thr	Gly	Met	Asp	Asn	Arg	Tyr	Leu	50	55	60	
15	Val	Leu	Ala	Val	Asn	Thr	Val	Gln	Asn	Lys	Glu	Gly	Asn	Cys	Glu	Lys	65	70	75	80
	Arg	Leu	Val	Ile	Thr	Ala	Ser	Gln	Ser	Leu	Glu	Asn	Lys	Glu	Leu	Cys	85	90	95	
20	Ile	Leu	Arg	Asn	Asp	Trp	Cys	Ser	Val	Pro	Val	Glu	Pro	Gly	Asp	Ile	100	105	110	
25	Ile	His	Leu	Glu	Gly	Asp	Cys	Thr	Ser	Asp	Thr	Trp	Ile	Ile	Asp	Lys	115	120	125	
	Asp	Phe	Gly	Tyr	Leu	Ile	Leu	Tyr	Pro	Asp	Met	Leu	Ile	Ser	Gly	Thr	130	135	140	
30	Ser	Ile	Ala	Ser	Ser	Ile	Arg	Cys	Met	Arg	Arg	Ala	Val	Leu	Ser	Glu	145	150	155	160
	Thr	Phe	Arg	Ser	Ser	Asp	Pro	Ala	Thr	Arg	Gln	Met	Leu	Ile	Gly	Thr	165	170	175	
35	Val	Leu	His	Glu	Val	Phe	Gln	Lys	Ala	Ile	Asn	Asn	Ser	Phe	Ala	Pro	180	185	190	
40	Glu	Lys	Leu	Gln	Glu	Leu	Ala	Phe	Gln	Thr	Ile	Gln	Glu	Ile	Arg	His	195	200	205	
	Leu	Lys	Glu	Met	Tyr	Arg	Leu	Asn	Leu	Ser	Gln	Asp	Glu	Ile	Lys	Gln	210	215	220	
45																				
	Glu	Val	Glu	Asp	Tyr	Leu	Pro	Ser	Phe	Cys	Lys	Trp	Ala	Gly	Asp	Phe	225	230	235	240
50	Met	His	Lys	Asn	Thr	Ser	Thr	Asp	Phe	Pro	Gln	Met	Gln	Leu	Ser	Leu	245	250	255	
	Pro	Ser	Asp	Asn	Ser	Lys	Asp	Asn	Ser	Thr	Cys	Asn	Ile	Glu	Val	Val	260	265	270	
55																				
	Lys	Pro	Met	Asp	Ile	Glu	Glu	Ser	Ile	Trp	Ser	Pro	Arg	Phe	Gly	Leu	275	280	285	
60	Lys	Gly	Lys	Ile	Asp	Val	Thr	Val	Gly	Val	Lys	Ile	His	Arg	Gly	Tyr	290	295	300	
	Lys	Thr	Lys	Tyr	Lys	Ile	Met	Pro	Leu	Glu	Leu	Lys	Thr	Gly	Lys	Glu	305	310	315	320

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	Ser	Asn	Ser	Ile	Glu	His	Arg	Ser	Gln	Val	Val	Leu	Tyr	Thr	Leu	Leu
					325					330					335	
5	Ser	Gln	Glu	Arg	Arg	Ala	Asp	Pro	Glu	Ala	Gly	Leu	Leu	Leu	Tyr	Leu
				340					345					350		
	Lys	Thr	Gly	Gln	Met	Tyr	Pro	Val	Pro	Ala	Asn	His	Leu	Asp	Lys	Arg
			355					360					365			
10	Glu	Leu	Leu	Lys	Leu	Arg	Asn	Gln	Met	Ala	Phe	Ser	Leu	Phe	His	Arg
		370					375					380				
	Ile	Ser	Lys	Ser	Ala	Thr	Arg	Gln	Lys	Thr	Gln	Leu	Ala	Ser	Leu	Pro
15		385				390					395					400
	Gln	Ile	Ile	Glu	Glu	Glu	Lys	Thr	Cys	Lys	Tyr	Cys	Ser	Gln	Ile	Gly
				405						410					415	
20	Asn	Cys	Ala	Leu	Tyr	Ser	Arg	Ala	Val	Glu	Gln	Gln	Met	Asp	Cys	Ser
				420					425					430		
	Ser	Val	Pro	Ile	Val	Met	Leu	Pro	Lys	Ile	Glu	Glu	Glu	Thr	Gln	His
25			435					440					445			
	Leu	Lys	Gln	Thr	His	Leu	Glu	Tyr	Phe	Ser	Leu	Trp	Cys	Leu	Met	Leu
		450					455					460				
30	Thr	Leu	Glu	Ser	Gln	Ser	Lys	Asp	Asn	Lys	Lys	Asn	His	Gln	Asn	Ile
	465					470					475					480
	Trp	Leu	Met	Pro	Ala	Ser	Glu	Met	Glu	Lys	Ser	Gly	Ser	Cys	Ile	Gly
				485					490						495	
35	Asn	Leu	Ile	Arg	Met	Glu	His	Val	Lys	Ile	Val	Cys	Asp	Gly	Gln	Tyr
				500					505					510		
	Leu	His	Asn	Phe	Gln	Cys	Lys	His	Gly	Ala	Ile	Pro	Val	Thr	Asn	Leu
40			515					520					525			
	Met	Ala	Gly	Asp	Arg	Val	Ile	Val	Ser	Gly	Glu	Glu	Arg	Ser	Leu	Phe
		530					535					540				
45	Ala	Leu	Ser	Arg	Gly	Tyr	Val	Lys	Glu	Ile	Asn	Met	Thr	Thr	Val	Thr
	545					550					555					560
	Cys	Leu	Leu	Asp	Arg	Asn	Leu	Ser	Val	Leu	Pro	Glu	Ser	Thr	Leu	Phe
				565						570					575	
50	Arg	Leu	Asp	Gln	Glu	Glu	Lys	Asn	Cys	Asp	Ile	Asp	Thr	Pro	Leu	Gly
				580					585					590		
55	Asn	Leu	Ser	Lys	Leu	Met	Glu	Asn	Thr	Phe	Val	Ser	Lys	Lys	Leu	Arg
			595					600					605			
	Asp	Leu	Ile	Ile	Asp	Phe	Arg	Glu	Pro	Gln	Phe	Ile	Ser	Tyr	Leu	Ser
60		610					615					620				
	Ser	Val	Leu	Pro	His	Asp	Ala	Lys	Asp	Thr	Val	Ala	Cys	Ile	Leu	Lys
		625				630					635					640
65	Gly	Leu	Asn	Lys	Pro	Gln	Arg	Gln	Ala	Met	Lys	Lys	Val	Leu	Leu	Ser
				645						650					655	
	Lys	Asp	Tyr	Thr	Leu	Ile	Val	Gly	Met	Pro	Gly	Thr	Gly	Lys	Thr	Thr
				660					665					670		

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	Thr	Ile	Cys	Thr	Leu	Val	Arg	Ile	Leu	Tyr	Ala	Cys	Gly	Phe	Ser	Val
			675					680					685			
5	Leu	Leu	Thr	Ser	Tyr	Thr	His	Ser	Ala	Val	Asp	Asn	Ile	Leu	Leu	Lys
	690						695					700				
	Leu	Ala	Lys	Phe	Lys	Ile	Gly	Phe	Leu	Arg	Leu	Gly	Gln	Ile	Gln	Lys
10	705					710					715					720
	Val	His	Pro	Ala	Ile	Gln	Gln	Phe	Thr	Glu	Gln	Glu	Ile	Cys	Arg	Ser
					725					730					735	
	Lys	Ser	Ile	Lys	Ser	Leu	Ala	Leu	Leu	Glu	Glu	Leu	Tyr	Asn	Ser	Gln
15				740					745					750		
	Leu	Ile	Val	Ala	Thr	Thr	Cys	Met	Gly	Ile	Asn	His	Pro	Ile	Phe	Ser
			755					760					765			
	Arg	Lys	Ile	Phe	Asp	Phe	Cys	Ile	Val	Asp	Glu	Ala	Ser	Gln	Ile	Ser
20		770					775					780				
	Gln	Pro	Ile	Cys	Leu	Gly	Pro	Leu	Phe	Phe	Ser	Arg	Arg	Phe	Val	Leu
25	785					790					795					800
	Val	Gly	Asp	His	Gln	Gln	Leu	Pro	Pro	Leu	Val	Leu	Asn	Arg	Glu	Ala
					805					810					815	
	Arg	Ala	Leu	Gly	Met	Ser	Glu	Ser	Leu	Phe	Lys	Arg	Leu	Glu	Gln	Asn
30				820					825					830		
	Lys	Ser	Ala	Val	Val	Gln	Leu	Thr	Val	Gln	Tyr	Arg	Met	Asn	Ser	Lys
			835					840					845			
	Ile	Met	Ser	Leu	Ser	Asn	Lys	Leu	Thr	Tyr	Glu	Gly	Lys	Leu	Glu	Cys
35		850					855					860				
	Gly	Ser	Asp	Lys	Val	Ala	Asn	Ala	Val	Ile	Asn	Leu	Arg	His	Phe	Lys
40	865					870					875					880
	Asp	Val	Lys	Leu	Glu	Leu	Glu	Phe	Tyr	Ala	Asp	Tyr	Ser	Asp	Asn	Pro
					885					890					895	
	Trp	Leu	Met	Gly	Val	Phe	Glu	Pro	Asn	Asn	Pro	Val	Cys	Phe	Leu	Asn
45			900						905					910		
	Thr	Asp	Lys	Val	Pro	Ala	Pro	Glu	Gln	Val	Glu	Lys	Gly	Gly	Val	Ser
			915					920					925			
50																
	Asn	Val	Thr	Glu	Ala	Lys	Leu	Ile	Val	Phe	Leu	Thr	Ser	Ile	Phe	Val
		930					935					940				
	Lys	Ala	Gly	Cys	Ser	Pro	Ser	Asp	Ile	Gly	Ile	Ile	Ala	Pro	Tyr	Arg
55	945					950					955					960
	Gln	Gln	Leu	Lys	Ile	Ile	Asn	Asp	Leu	Leu	Ala	Arg	Ser	Ile	Gly	Met
60					965					970					975	
	Val	Glu	Val	Asn	Thr	Val	Asp	Lys	Tyr	Gln	Gly	Arg	Asp	Lys	Ser	Ile
				980					985					990		
	Val	Leu	Val	Ser	Phe	Val	Arg	Ser	Asn	Lys	Asp	Gly	Thr	Val	Gly	Glu
65				995				1000						1005		

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Leu Leu Lys Asp Trp Arg Arg Leu Asn Val Ala Ile Thr Arg Ala Lys
 1010 1015 1020
 5 His Lys Leu Ile Leu Leu Gly Cys Val Pro Ser Leu Asn Cys Tyr Pro
 1025 1030 1035 1040
 Pro Leu Glu Lys Leu Leu Asn His Leu Asn Ser Glu Lys Leu Ile Ile
 1045 1050 1055
 10 Asp Leu Pro Ser Arg Glu His Glu Ser Leu Cys His Ile Leu Gly Asp
 1060 1065 1070
 Phe Gln Arg Glu
 1075
 15

(2) INFORMATION FOR SEQ ID NO: 13:

(i) SEQUENCE CHARACTERISTICS:
 20 (A) LENGTH: 527 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 25 (ii) MOLECULE TYPE: protein
 (iii) HYPOTHETICAL: NO
 (iv) ANTI-SENSE: NO
 30 (vi) ORIGINAL SOURCE:
 (A) ORGANISM: homo sapiens
 35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:
 Met Ala Asp Ser Arg Asp Pro Ala Ser Asp Gln Met Gln His Trp Lys
 1 5 10 15
 40 Glu Gln Arg Ala Ala Gln Lys Ala Asp Val Leu Thr Thr Gly Ala Gly
 20 25 30
 Asn Pro Val Gly Asp Lys Leu Asn Val Ile Thr Val Gly Pro Arg Gly
 35 40 45
 45 Pro Leu Leu Val Gln Asp Val Val Phe Thr Asp Glu Met Ala His Phe
 50 55 60
 50 Asp Arg Glu Arg Ile Pro Glu Arg Val Val His Ala Lys Gly Ala Gly
 65 70 75 80
 Ala Phe Gly Tyr Phe Glu Val Thr His Asp Ile Thr Lys Tyr Ser Lys
 85 90 95
 55 Ala Lys Val Phe Glu His Ile Gly Lys Lys Thr Pro Ile Ala Val Arg
 100 105 110
 60 Phe Ser Thr Val Ala Gly Glu Ser Gly Ser Ala Asp Thr Val Arg Asp
 115 120 125
 Pro Arg Gly Phe Ala Val Lys Phe Tyr Thr Glu Asp Gly Asn Trp Asp
 130 135 140
 65 Leu Val Gly Asn Asn Thr Pro Ile Phe Phe Ile Arg Asp Pro Ile Leu
 145 150 155 160

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	Phe	Pro	Ser	Phe	Ile	His	Ser	Gln	Lys	Arg	Asn	Pro	Gln	Thr	His	Leu
					165					170					175	
5	Lys	Asp	Pro	Asp	Met	Val	Trp	Asp	Phe	Trp	Ser	Leu	Arg	Pro	Glu	Ser
				180					185					190		
	Leu	His	Gln	Val	Ser	Phe	Leu	Phe	Ser	Asp	Arg	Gly	Ile	Pro	Asp	Gly
			195					200					205			
10	His	Arg	His	Met	Asn	Gly	Tyr	Gly	Ser	His	Thr	Phe	Lys	Leu	Val	Asn
		210					215					220				
	Ala	Asn	Gly	Glu	Ala	Val	Tyr	Cys	Lys	Phe	His	Tyr	Lys	Thr	Asp	Gln
15	225					230					235					240
	Gly	Ile	Lys	Asn	Leu	Ser	Val	Glu	Asp	Ala	Ala	Arg	Leu	Ser	Gln	Glu
				245						250					255	
20	Asp	Pro	Asp	Tyr	Gly	Ile	Arg	Asp	Leu	Phe	Asn	Ala	Ile	Ala	Thr	Gly
				260					265					270		
	Lys	Tyr	Pro	Ser	Trp	Thr	Phe	Tyr	Ile	Gln	Val	Met	Thr	Phe	Asn	Gln
			275					280					285			
25	Ala	Glu	Thr	Phe	Pro	Phe	Asn	Pro	Phe	Asp	Leu	Thr	Lys	Val	Trp	Pro
		290					295					300				
	His	Lys	Asp	Tyr	Pro	Leu	Ile	Pro	Val	Gly	Lys	Leu	Val	Leu	Asn	Arg
30	305					310					315					320
	Asn	Pro	Val	Asn	Tyr	Phe	Ala	Glu	Val	Glu	Gln	Ile	Ala	Phe	Asp	Pro
				325						330					335	
35	Ser	Asn	Met	Pro	Pro	Gly	Ile	Glu	Ala	Ser	Pro	Asp	Lys	Met	Leu	Gln
				340					345					350		
	Gly	Arg	Leu	Phe	Ala	Tyr	Pro	Asp	Thr	His	Arg	His	Arg	Leu	Gly	Pro
			355					360					365			
40	Asn	Tyr	Leu	His	Ile	Pro	Val	Asn	Cys	Pro	Tyr	Arg	Ala	Arg	Val	Ala
		370					375					380				
	Asn	Tyr	Gln	Arg	Asp	Gly	Pro	Met	Cys	Met	Gln	Asp	Asn	Gln	Gly	Gly
45	385					390					395					400
	Ala	Pro	Asn	Tyr	Tyr	Pro	Asn	Ser	Phe	Gly	Ala	Pro	Glu	Gln	Gln	Pro
					405					410					415	
50	Ser	Ala	Leu	Glu	His	Ser	Ile	Gln	Tyr	Ser	Gly	Glu	Val	Arg	Arg	Phe
				420					425					430		
	Asn	Thr	Ala	Asn	Asp	Asp	Asn	Val	Thr	Gln	Val	Arg	Ala	Phe	Tyr	Val
55			435					440					445			
	Asn	Val	Leu	Asn	Glu	Glu	Gln	Arg	Lys	Arg	Leu	Cys	Glu	Asn	Ile	Ala
		450					455					460				
60	Gly	His	Leu	Lys	Asp	Ala	Gln	Ile	Phe	Ile	Gln	Lys	Lys	Ala	Val	Lys
	465					470					475					480
	Asn	Phe	Thr	Glu	Val	His	Pro	Asp	Tyr	Gly	Ser	His	Ile	Gln	Ala	Leu
					485					490					495	
65	Leu	Asp	Lys	Tyr	Asn	Ala	Glu	Lys	Pro	Lys	Asn	Ala	Ile	His	Thr	Phe
				500					505					510		

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Val Gln Ser Gly Ser His Leu Ala Ala Arg Glu Lys Ala Asn Leu
 515 520 525

5 (2) INFORMATION FOR SEQ ID NO: 14:

(i) SEQUENCE CHARACTERISTICS:

10 (A) LENGTH: 353 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

15 (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

20 (A) ORGANISM: homo sapiens

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

25 Met Glu Lys Thr Leu Glu Thr Val Pro Leu Glu Arg Lys Lys Arg Glu
 1 5 10 15
 30 Lys Glu Gln Phe Arg Lys Leu Phe Ile Gly Gly Leu Ser Phe Glu Thr
 20 25 30
 Thr Glu Glu Ser Leu Arg Asn Tyr Tyr Glu Gln Trp Gly Lys Leu Thr
 35 35 40 45
 Asp Cys Val Val Met Arg Asp Pro Ala Ser Lys Arg Ser Arg Gly Phe
 50 55 60
 40 Gly Phe Val Thr Phe Ser Ser Met Ala Glu Val Asp Ala Ala Met Ala
 65 70 75 80
 Ala Arg Pro His Ser Ile Asp Gly Arg Val Val Glu Pro Lys Arg Ala
 85 90 95
 45 Val Ala Arg Glu Glu Ser Gly Lys Pro Gly Ala His Val Thr Val Lys
 100 105 110
 Lys Leu Phe Val Gly Gly Ile Lys Glu Asp Thr Glu Glu His His Leu
 115 120 125
 50 Arg Asp Tyr Phe Glu Glu Tyr Gly Lys Ile Asp Thr Ile Glu Ile Ile
 130 135 140
 55 Thr Asp Arg Gln Ser Gly Lys Lys Arg Gly Phe Gly Phe Val Thr Phe
 145 150 155 160
 Asp Asp His Asp Pro Val Asp Lys Ile Val Leu Gln Lys Tyr His Thr
 60 165 170 175
 Ile Asn Gly His Asn Ala Glu Val Arg Lys Ala Leu Ser Arg Gln Glu
 180 185 190
 65 Met Gln Glu Val Gln Ser Ser Arg Ser Gly Arg Gly Gly Asn Phe Gly
 195 200 205
 Phe Gly Asp Ser Arg Gly Gly Gly Gly Asn Phe Gly Pro Gly Pro Gly
 210 215 220

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Ser Asn Phe Arg Gly Gly Ser Asp Gly Tyr Gly Ser Gly Arg Gly Phe
 225 230 235 240
 5 Gly Asp Gly Tyr Asn Gly Tyr Gly Gly Gly Pro Gly Gly Gly Asn Phe
 245 250 255
 Gly Gly Ser Pro Gly Tyr Gly Gly Gly Arg Gly Gly Tyr Gly Gly Gly
 260 265 270
 10 Gly Pro Gly Tyr Gly Asn Gln Gly Gly Gly Tyr Gly Gly Gly Tyr Asp
 275 280 285
 Asn Tyr Gly Gly Gly Asn Tyr Gly Ser Gly Asn Tyr Asn Asp Phe Gly
 290 295 300
 15 Asn Tyr Asn Gln Gln Pro Ser Asn Tyr Gly Pro Met Lys Ser Gly Asn
 305 310 315 320
 20 Phe Gly Gly Ser Arg Asn Met Gly Gly Pro Tyr Gly Gly Gly Asn Tyr
 325 330 335
 Gly Pro Gly Gly Ser Gly Gly Ser Gly Tyr Gly Gly Arg Ser Arg
 340 345 350
 25 Tyr

(2) INFORMATION FOR SEQ ID NO: 15:

30 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 194 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 35 (D) TOPOLOGY: linear
 (ii) MOLECULE TYPE: protein
 (iii) HYPOTHETICAL: NO
 40 (iv) ANTI-SENSE: NO
 (vi) ORIGINAL SOURCE:
 (A) ORGANISM: homo sapiens
 45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 15:

50 Met Ala Ala Glu Asp Val Ala Ala Thr Gly Ala Asp Pro Ser Glu Leu
 1 5 10 15
 55 Glu Gly Gly Gly Leu Leu His Glu Ile Phe Thr Ser Pro Leu Asn Leu
 20 25 30
 Leu Leu Leu Gly Leu Cys Ile Phe Leu Leu Tyr Lys Ile Val Arg Gly
 35 40 45
 60 Asp Gln Pro Ala Ala Ser Asp Ser Asp Asp Glu Pro Pro Pro Leu
 50 55 60
 Pro Arg Leu Lys Arg Arg Asp Phe Thr Pro Ala Glu Leu Arg Arg Phe
 65 70 75 80
 65 Asp Gly Val Gln Asp Pro Arg Ile Leu Met Ala Ile Asn Gly Lys Val
 85 90 95

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Phe Asp Val Thr Lys Gly Arg Lys Phe Tyr Gly Pro Glu Gly Pro Tyr
 100 105 110
 5 Gly Val Phe Ala Gly Arg Asp Ala Ser Arg Gly Leu Ala Thr Phe Cys
 115 120 125
 Leu Asp Lys Glu Ala Leu Lys Asp Glu Tyr Asp Asp Leu Ser Asp Leu
 130 135 140
 10 Thr Pro Ala Gln Gln Glu Thr Leu Asn Asp Trp Asp Ser Gln Phe Thr
 145 150 155 160
 Phe Lys Tyr His His Val Gly Lys Leu Leu Lys Glu Gly Glu Glu Pro
 165 170 175
 15 Thr Val Tyr Ser Asp Glu Glu Glu Pro Lys Asp Glu Ser Ala Arg Lys
 180 185 190
 20 Asn Asp

(2) INFORMATION FOR SEQ ID NO: 16:

25 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 646 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 30 (ii) MOLECULE TYPE: protein
 (iii) HYPOTHETICAL: NO
 35 (iv) ANTI-SENSE: NO
 (vi) ORIGINAL SOURCE:
 (A) ORGANISM: homo sapiens
 40
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:
 45 Met Ser Lys Gly Pro Ala Val Gly Ile Asp Leu Gly Thr Thr Tyr Ser
 1 5 10 15
 Cys Val Gly Val Phe Gln His Gly Lys Val Glu Ile Ile Ala Asn Asp
 20 25 30
 50 Gln Gly Asn Arg Thr Thr Pro Ser Tyr Val Ala Phe Thr Asp Thr Glu
 35 40 45
 55 Arg Leu Ile Gly Asp Ala Ala Lys Asn Gln Val Ala Met Asn Pro Thr
 50 55 60
 Asn Thr Val Phe Asp Ala Lys Arg Leu Ile Gly Arg Arg Phe Asp Asp
 65 70 75 80
 60 Ala Val Val Gln Ser Asp Met Lys His Trp Pro Phe Met Val Val Asn
 85 90 95
 65 Asp Ala Gly Arg Pro Lys Val Gln Val Glu Tyr Lys Gly Glu Thr Lys
 100 105 110
 Ser Phe Tyr Pro Glu Glu Val Ser Met Val Leu Thr Lys Met Lys
 115 120 125

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	Glu	Ile	Ala	Glu	Ala	Tyr	Leu	Gly	Lys	Thr	Val	Thr	Asn	Ala	Val	Val	
	130						135					140					
5	Thr	Val	Pro	Ala	Tyr	Phe	Asn	Asp	Ser	Gln	Arg	Gln	Ala	Thr	Lys	Asp	
	145					150					155					160	
	Ala	Gly	Thr	Ile	Ala	Gly	Leu	Asn	Val	Leu	Arg	Ile	Ile	Asn	Glu	Pro	
10					165					170					175		
	Thr	Ala	Ala	Ala	Ile	Ala	Tyr	Gly	Leu	Asp	Lys	Lys	Val	Gly	Ala	Glu	
				180				185						190			
15	Arg	Asn	Val	Leu	Ile	Phe	Asp	Leu	Gly	Gly	Gly	Thr	Phe	Asp	Val	Ser	
			195					200					205				
	Ile	Leu	Thr	Ile	Glu	Asp	Gly	Ile	Phe	Glu	Val	Lys	Ser	Thr	Ala	Gly	
	210					215						220					
20	Asp	Thr	His	Leu	Gly	Gly	Glu	Asp	Phe	Asp	Asn	Arg	Met	Val	Asn	His	
	225				230						235					240	
	Phe	Ile	Ala	Glu	Phe	Lys	Arg	Lys	His	Lys	Lys	Asp	Ile	Ser	Glu	Asn	
25					245					250					255		
	Lys	Arg	Ala	Val	Arg	Arg	Leu	Arg	Thr	Ala	Cys	Glu	Arg	Ala	Lys	Arg	
				260					265					270			
30	Thr	Leu	Ser	Ser	Ser	Thr	Gln	Ala	Ser	Ile	Glu	Ile	Asp	Ser	Leu	Tyr	
			275					280					285				
	Glu	Gly	Ile	Asp	Phe	Tyr	Thr	Ser	Ile	Thr	Arg	Ala	Arg	Phe	Glu	Glu	
	290					295						300					
35	Leu	Asn	Ala	Asp	Leu	Phe	Arg	Gly	Thr	Leu	Asp	Pro	Val	Glu	Lys	Ala	
	305					310					315					320	
	Leu	Arg	Asp	Ala	Lys	Leu	Asp	Lys	Ser	Gln	Ile	His	Asp	Ile	Val	Leu	
40					325					330					335		
	Val	Gly	Gly	Ser	Thr	Arg	Ile	Pro	Lys	Ile	Gln	Lys	Leu	Leu	Gln	Asp	
				340					345					350			
45	Phe	Phe	Asn	Gly	Lys	Glu	Leu	Asn	Lys	Ser	Ile	Asn	Pro	Asp	Glu	Ala	
			355					360					365				
	Val	Ala	Tyr	Gly	Ala	Ala	Val	Gln	Ala	Ala	Ile	Leu	Ser	Gly	Asp	Lys	
	370					375						380					
50	Ser	Glu	Asn	Val	Gln	Asp	Leu	Leu	Leu	Leu	Asp	Val	Thr	Pro	Leu	Ser	
	385					390					395					400	
	Leu	Gly	Ile	Glu	Thr	Ala	Gly	Gly	Val	Met	Thr	Val	Leu	Ile	Lys	Arg	
55					405					410					415		
	Asn	Thr	Thr	Ile	Pro	Thr	Lys	Gln	Thr	Gln	Thr	Phe	Thr	Thr	Tyr	Ser	
				420					425					430			
60	Asp	Asn	Gln	Pro	Gly	Val	Leu	Ile	Gln	Val	Tyr	Glu	Gly	Glu	Arg	Ala	
			435					440					445				
	Met	Thr	Lys	Asp	Asn	Asn	Leu	Leu	Gly	Lys	Phe	Glu	Leu	Thr	Gly	Ile	
65		450					455					460					
	Pro	Pro	Ala	Pro	Arg	Gly	Val	Pro	Gln	Ile	Glu	Val	Thr	Phe	Asp	Ile	
	465					470					475					480	

[illegible]

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CLAIMS

5 1. A method of characterising a biological sample
 comprising detecting or quantitating therein one or more
 proteins produced by the endometrium in increased amounts in
 hyperplasia or in adenocarcinoma as shown by 2D gel
 electrophoresis comparison of cell lysates of endometrial
 10 biopsies from normal endometrium and endometrium showing
 hyperplasia or adenocarcinoma, excluding variations due to
 the menstrual cycle, or detecting or quantitating a fragment
 or breakdown product thereof, or a nucleic acid coding
 therefor or antibodies thereto.

15

2. A method of characterising a biological sample
 comprising detecting or quantitating therein one or more
 proteins produced by the endometrium in increased amounts in
 hyperplasia or in adenocarcinoma and characterised by one of
 20 the following combinations of molecular weight and pI
 values:

	hyperplasia	
	pI	MW kDa
25	6.7	91
	6.6	90
	6.9	64
	6.6	67
	6.3	66
30	6.8	46
	5.7	41
	5.5	35
	5.3	13
	6.6	101
35	5.8	14
	7.4	51
	8.2	44
	9.5	48

40

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	adenocarcinoma	
	pI	MW (kDa)
5	6.3	32
	6.0	109
	6.7	91
	6.6	90
10	6.9	64
	6.6	67
	6.3	66
	6.2	62
	6.2	45
15	5.7	45
	5.4	33
	6.3	27
	6.5	103
	6.8	90
20	6.9	78
	5.3	13
	6.2	130
	6.3	66
	6.3	73
25	8.3	32
	8.1	55
	8.2	44
	6.6	111
	7.7	43
30	9.5	48
	8.3	32
	7.7	39

or a fragment or breakdown product thereof, or a nucleic
 35 acid coding therefor or antibodies thereto.

3. A method as claimed in Claim 1 or Claim 2, wherein said
 protein, fragment, breakdown product, antibodies, or nucleic
 acid is detected in a body fluid sample.

4. An immunological binding partner specifically reactive
with a protein as defined in Claim 1 or Claim 2 or with a
5 fragment or breakdown product thereof or with a nucleic acid
coding therefor.

5. A cell line producing a monoclonal antibody being an
immunological binding partner as claimed in Claim 4.

10

6. An assay kit for use in a method as claimed in Claim 1
or Claim 2, comprising an immunological binding partner as
claimed in Claim 4.

15 7. A method of characterising a biological sample com-
prising detecting or quantitating therein one or more
proteins produced by the endometrium in increased amounts
during the proliferative phase of the endometrium as shown
in 2D gel electrophoresis comparison of cell lysates of
20 endometrial biopsies from normal endometrium in its
proliferative and secretory phases and characterised by one
of the following combinations of molecular weight and pI
values:-

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pI	MW (kDa)
6.9	86
5.4	34
5.6	67
5.3	23
6.8	52
8.7	47
8.2	138
6.5	124
7.7	119
7.8	119
8.1	66
7.1	58
6.8	66
7.9	48
7.7	31
6.8	29
7.2	70
8.0	119
6.7	62

or a fragment or breakdown product thereof, or a nucleic
5 acid coding therefor, or an antibody thereto.

8. A method as claimed in Claim 7, for detecting the phase
of the endometrium.

10 9. A method as claimed in Claim 7 or Claim 8, wherein said
protein, fragment, or breakdown product is detected in a
body fluid sample.

15 10. An immunological binding partner specifically reactive
with a protein as defined in Claim 7 or with a fragment or
breakdown product thereof or with a nucleic acid coding
therefor.

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11. A cell line producing a monoclonal antibody being an immunological binding partner as claimed in Claim 10.
- 125 12. An assay kit for use in a method as claimed in Claim 7 or Claim 8, comprising an immunological binding partner as claimed in Claim 10.
- 10 13. A protein produced by the endometrium in increased amounts in hyperplasia or in adenocarcinoma as shown by 2D gel electrophoresis comparison of cell lysates of endo-metrial biopsies from normal endometrium and endometrium showing hyperplasia or adenocarcinoma, excluding variations due to the menstrual cycle, and
- 15 characterised by one of the following combinations of molecular weight and pI values:

hyperplasia		
	pI	MW kDa
20	6.7	91
	6.6	90
	6.9	64
	6.8	46
	5.7	41
25	5.3	13
	6.6	101
	5.8	14
	9.5	48

30

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adenocarcinoma		
	pI	MW (kDa)
5	6.3	32
	6.0	109
	6.7	91
	6.6	90
	6.9	64
10	6.2	62
	6.5	103
	6.8	90
	5.3	13
	6.2	130
15	6.3	66
	6.3	73
	8.3	32
	8.1	55
	6.6	111
20	7.7	43
	9.5	48
	8.3	32

14. A protein produced by the endometrium in increased amounts during the proliferative phase of the endometrium as shown in 2D gel electrophoresis comparison of cell lysates of endometrial biopsies from normal endometrium in its proliferative and secretory phases and characterised by one of the following combinations of molecular weight and pI values:-

30

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pI	MW (kDa)
6.9	86
5.6	67
6.8	52
8.2	138
6.5	124
7.7	119
7.8	119
8.1	66
7.1	58
6.8	66
7.7	31

15. A protein as claimed in Claim 13 or Claim 14,
5 characterised by the properties:-

PI	MW(kDa)
5.7	41
5.6	67
9.5	48
6.8	52
6.5	124
7.7	119
7.8	119

and by the respective tryptic digestion MS spectra shown in
Figures 7 to 12.

10

16. The use of a protein as defined in any one of Claims 1,
2 or 7 or a fragment thereof, for detecting autoantibodies
to a said protein.

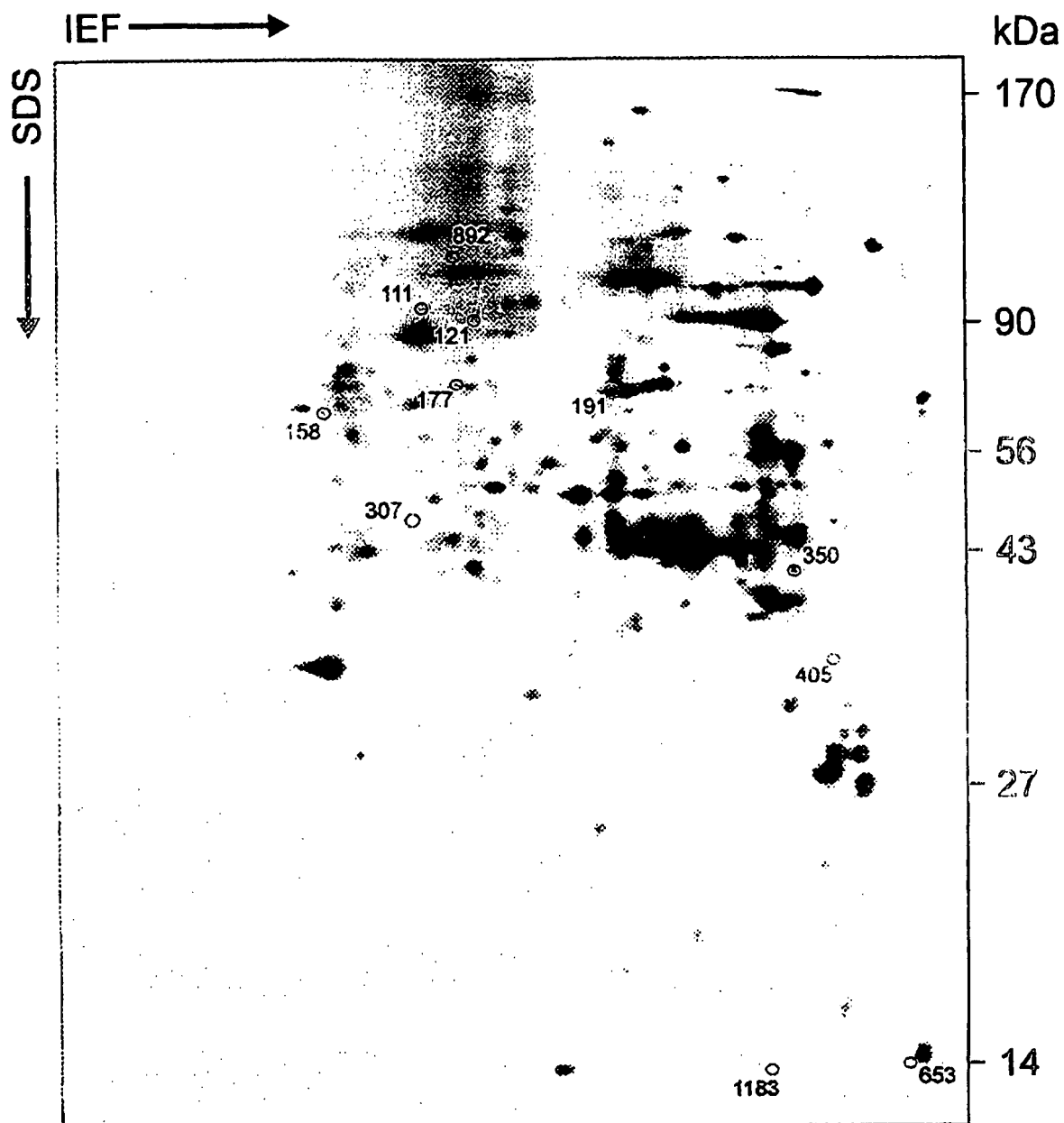


FIG. 1

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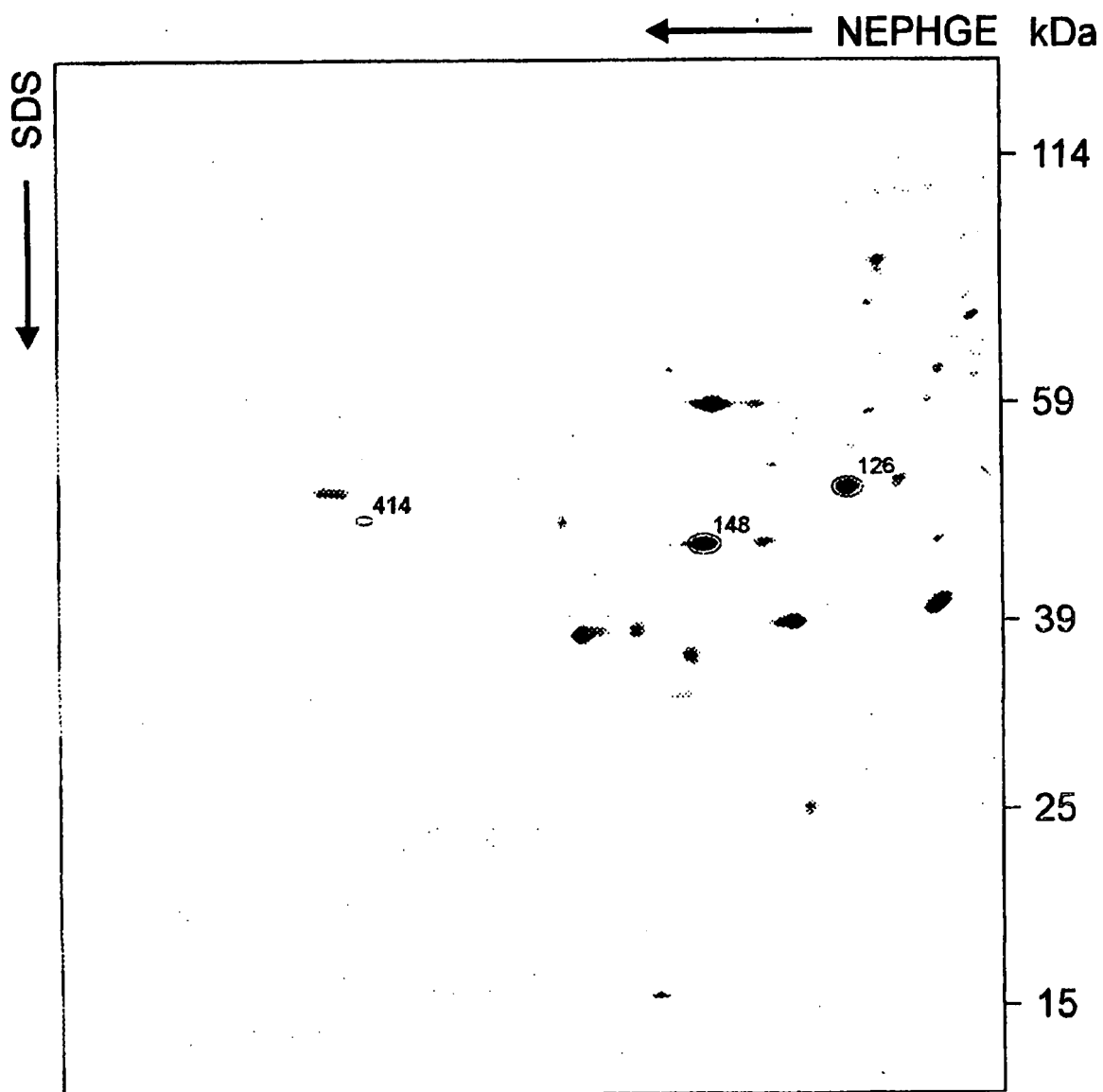


Fig. 2

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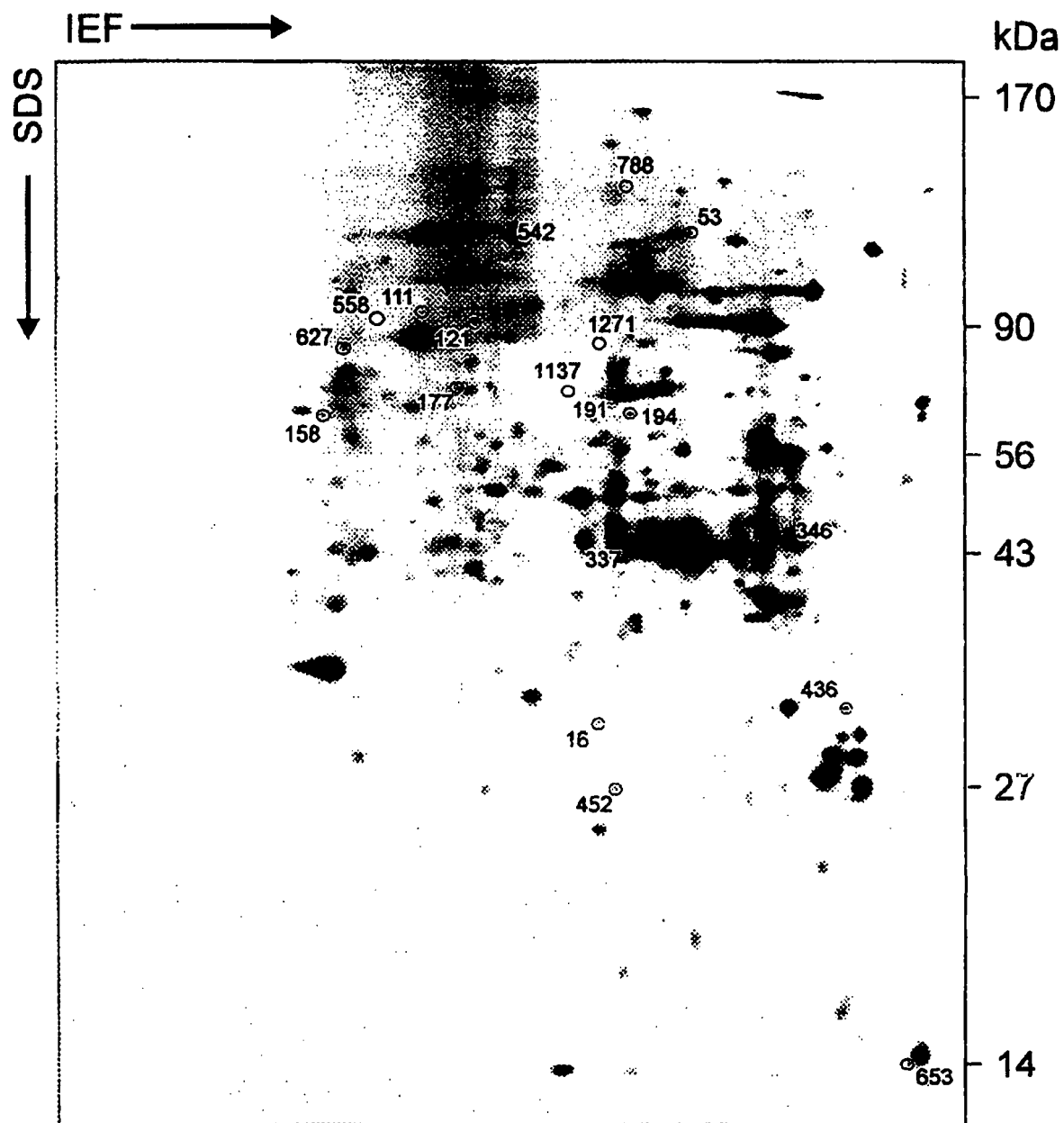


FIG. 3

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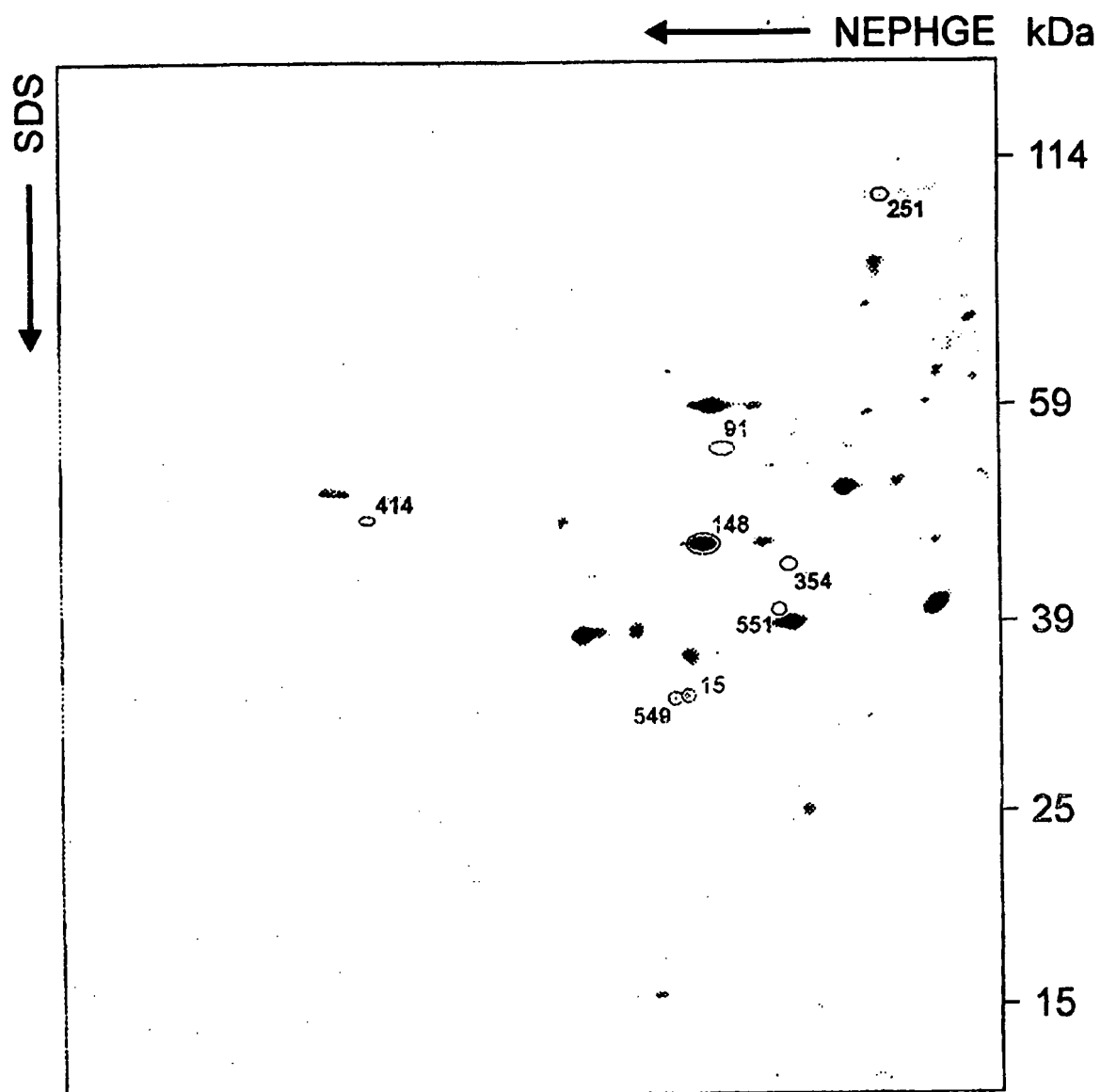
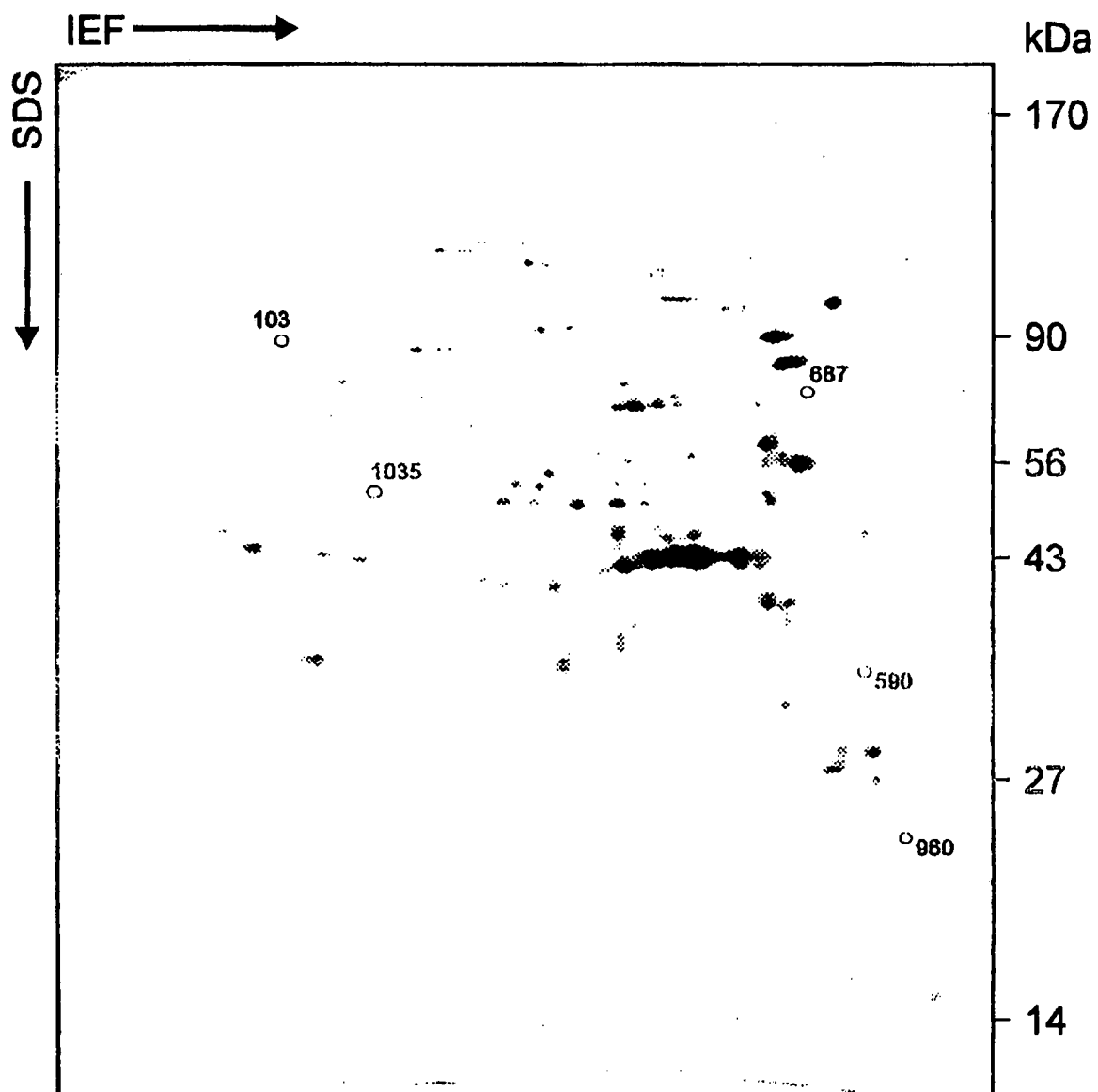
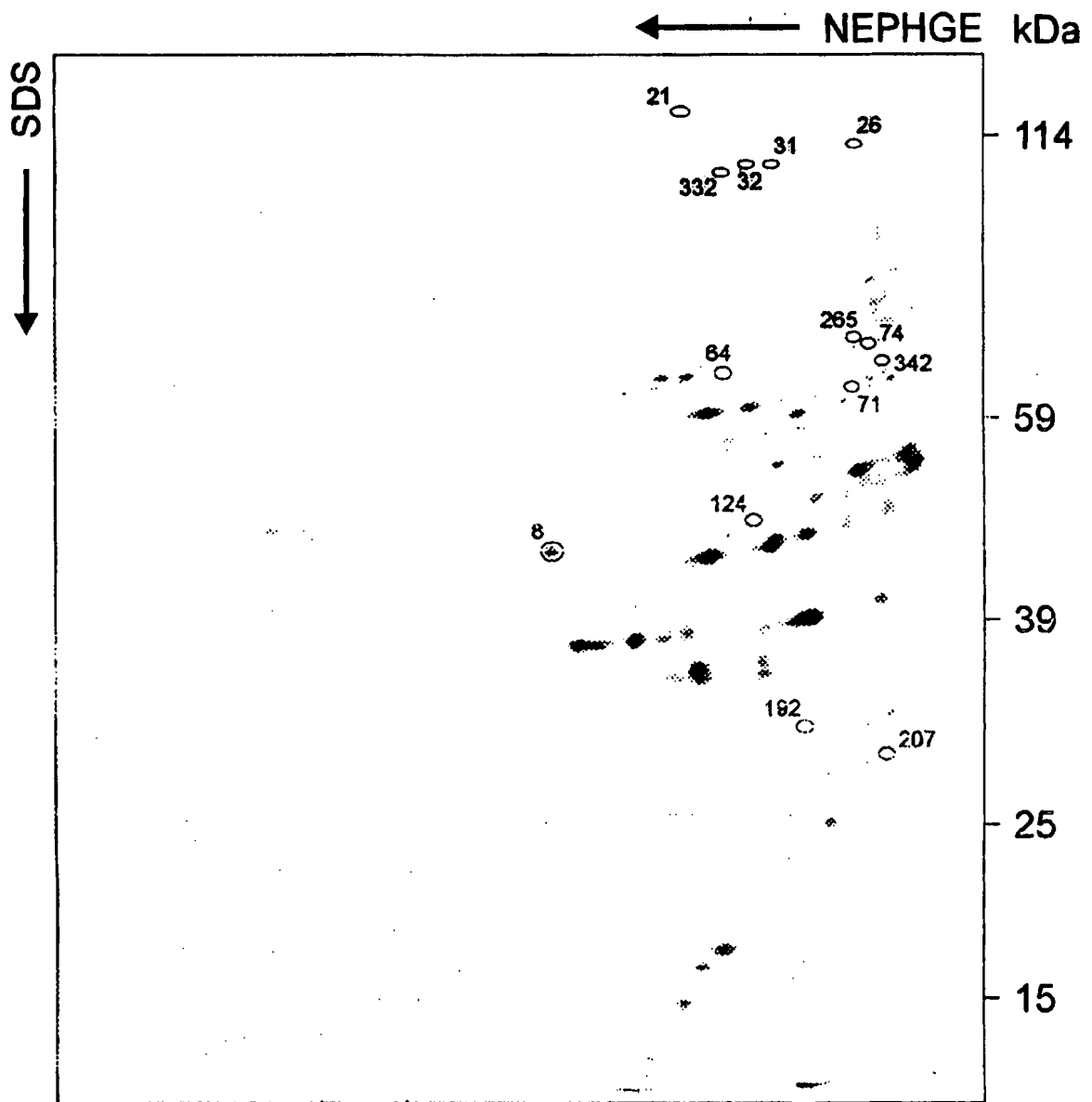


Fig. 4

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*Fig. 5*

*Fig. 6*

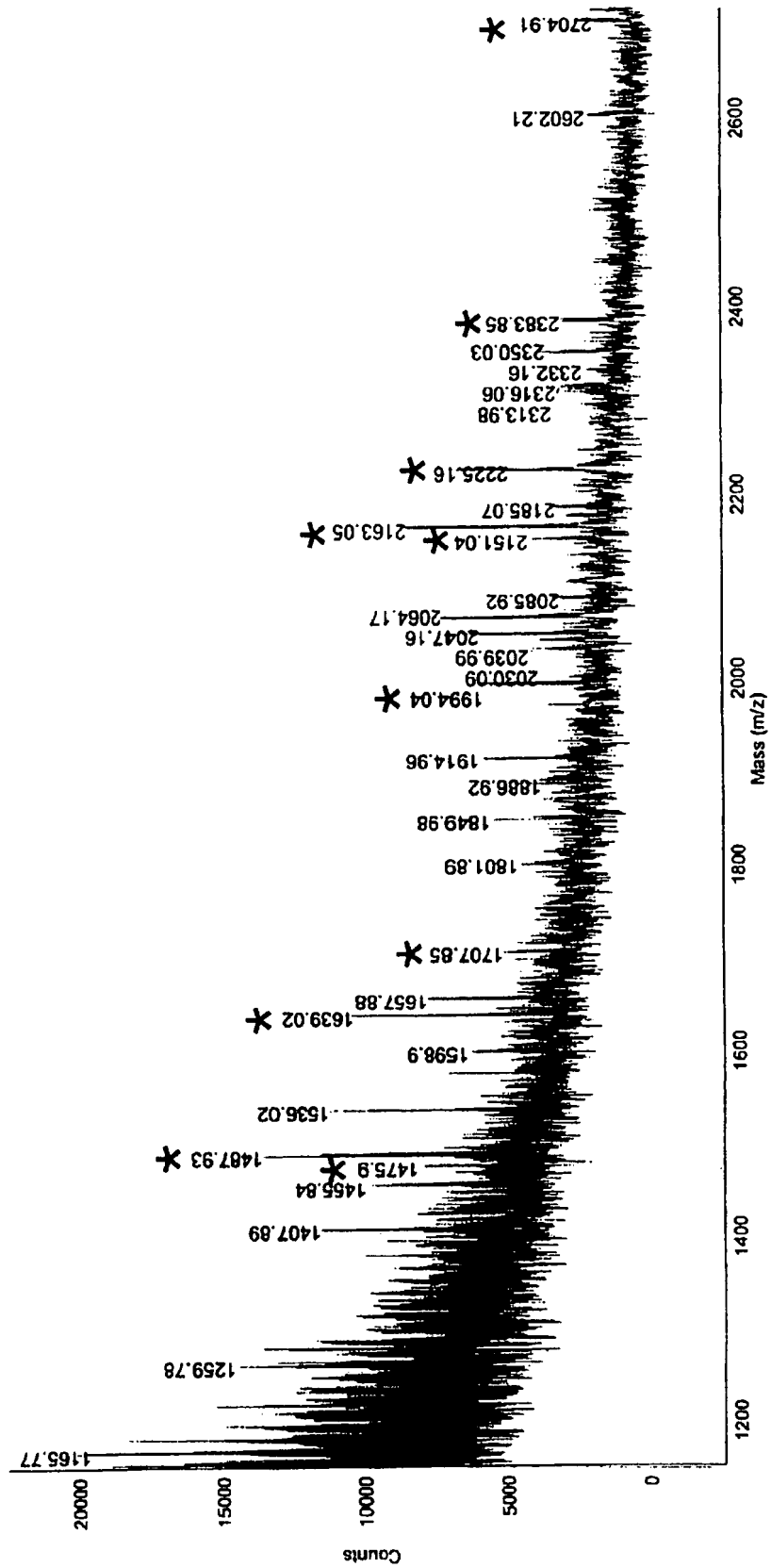


Fig 7

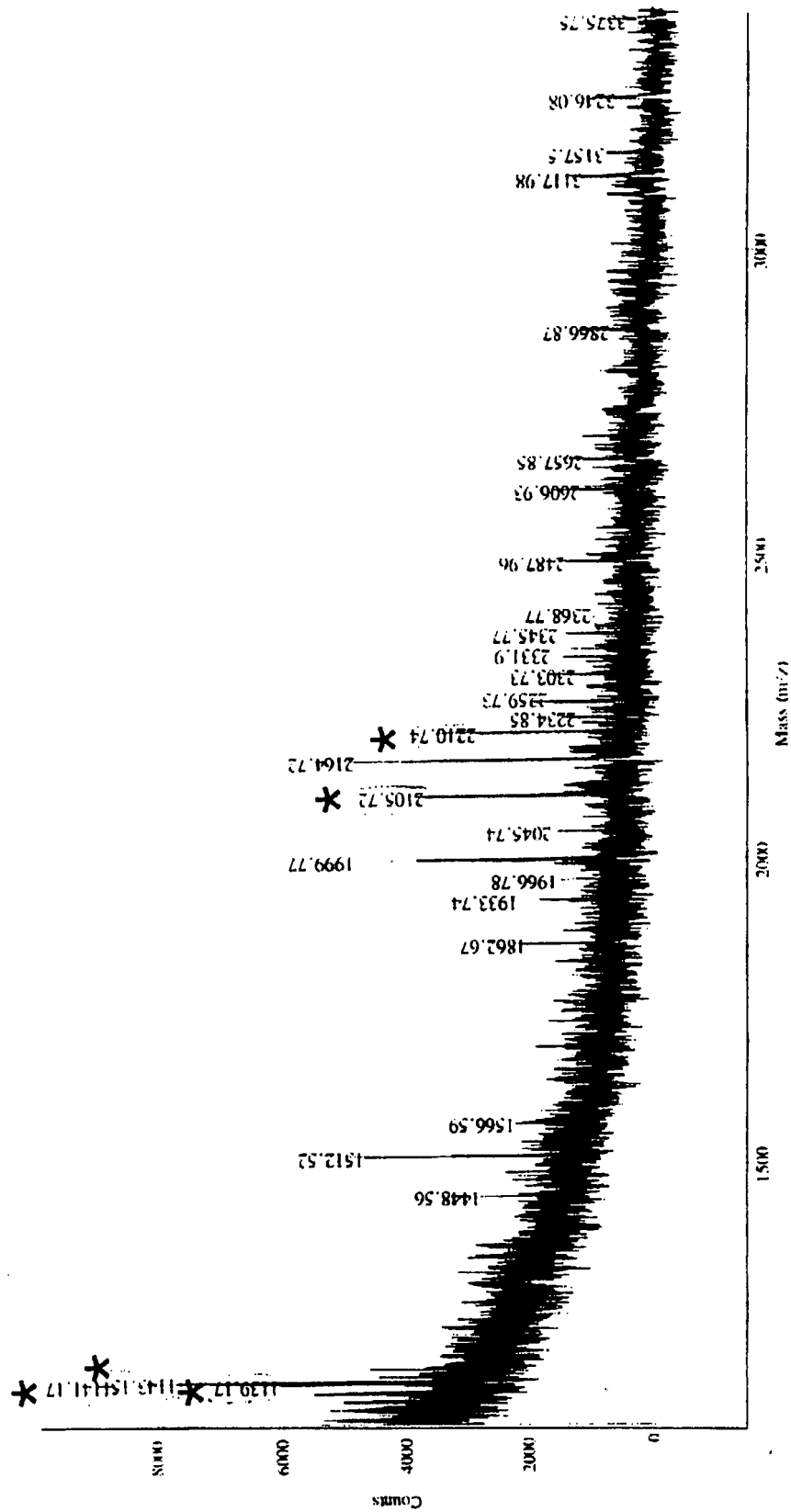


Fig 8

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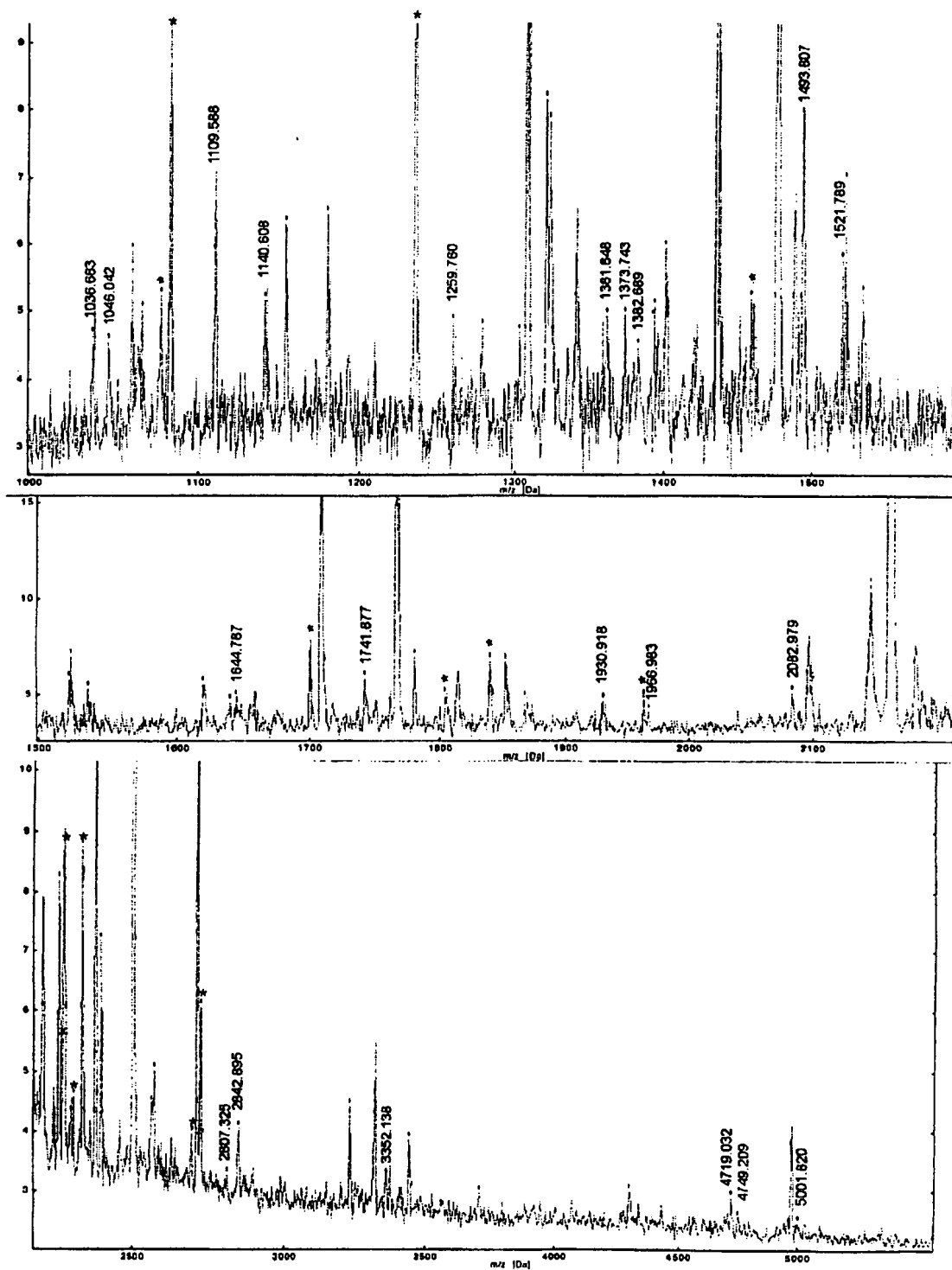


FIG. 9

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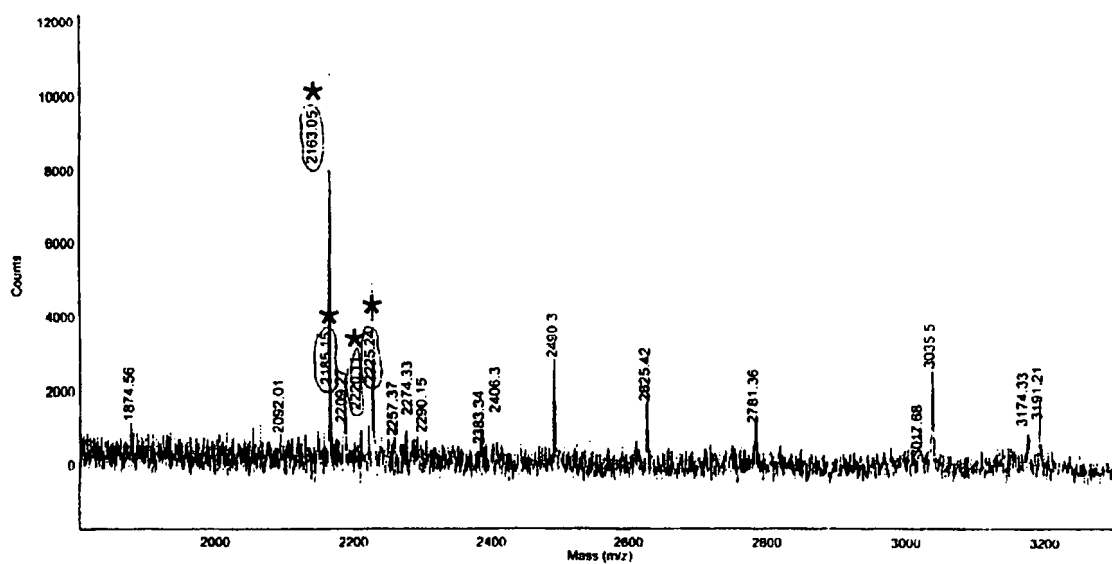
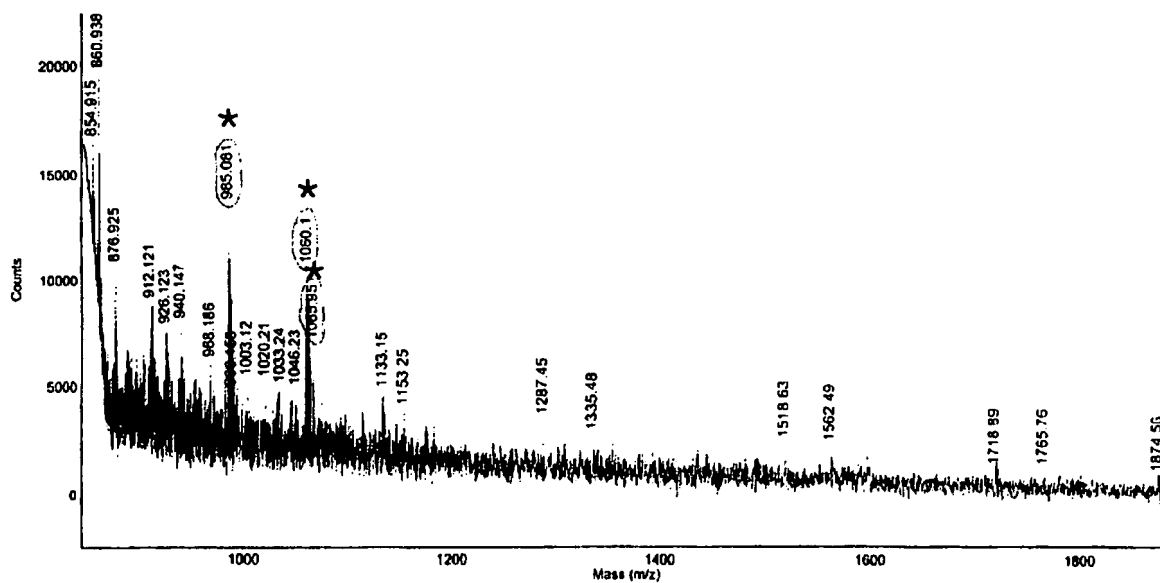


FIG. 10

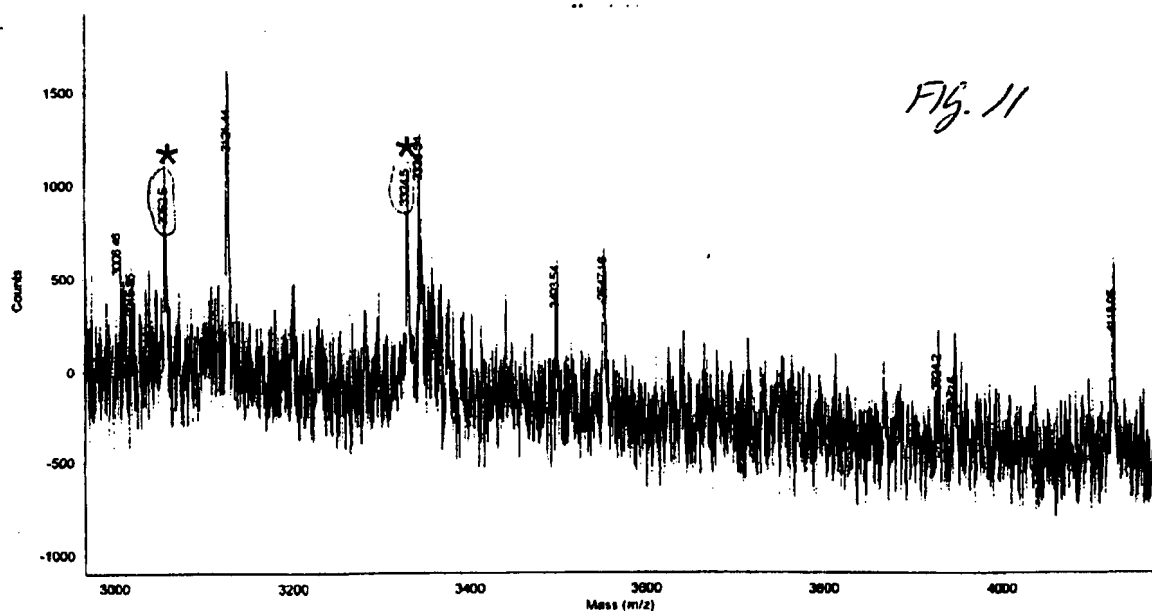
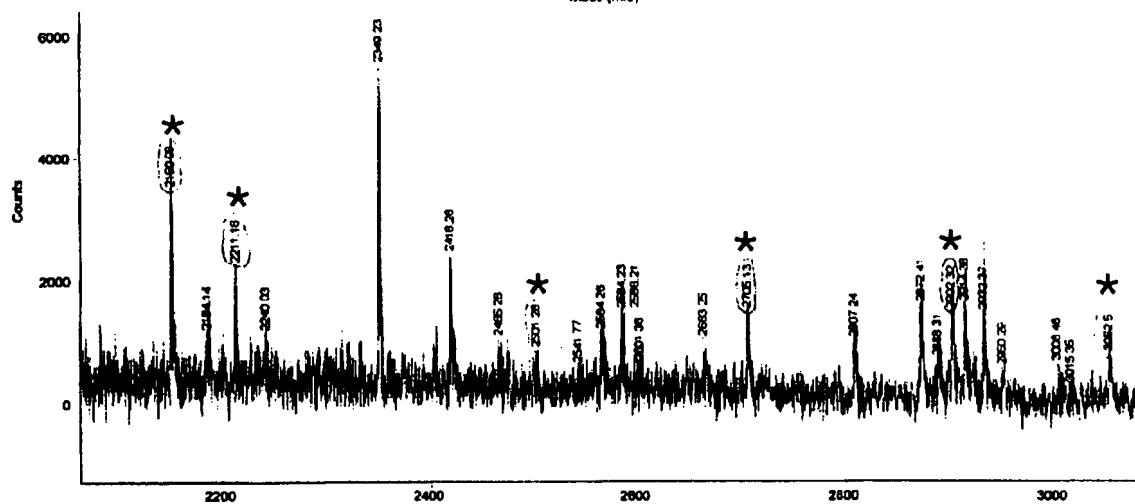
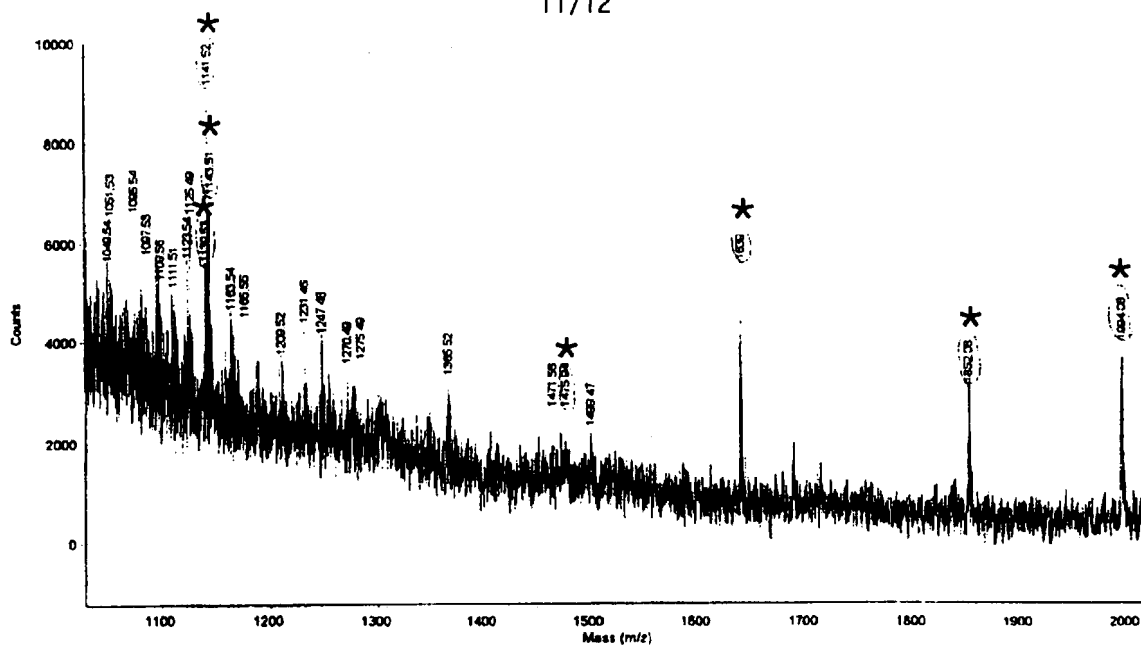


Fig. 11

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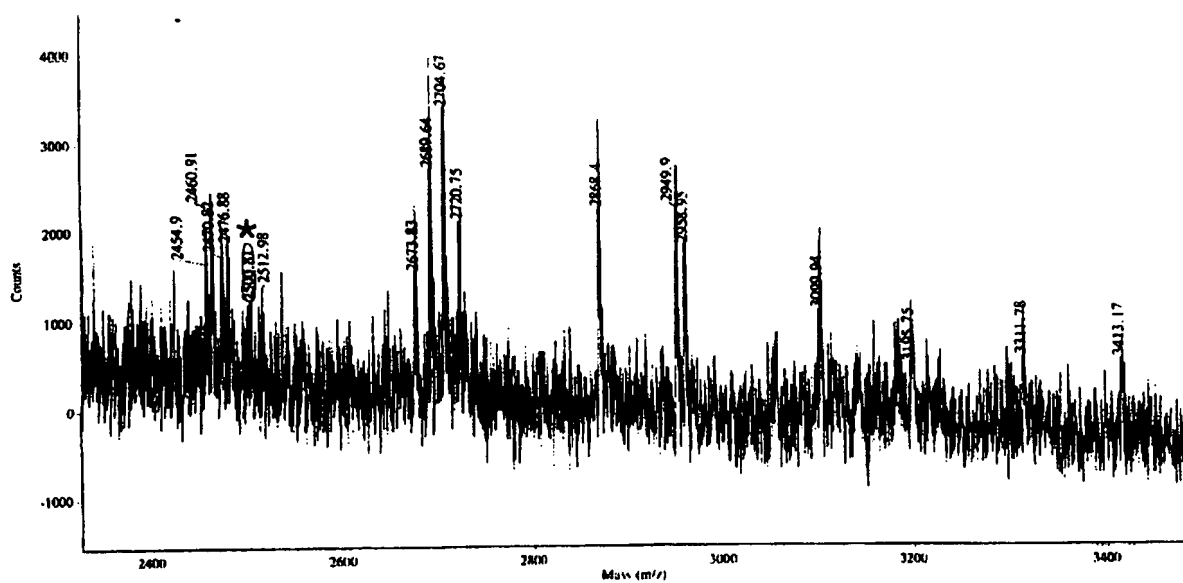
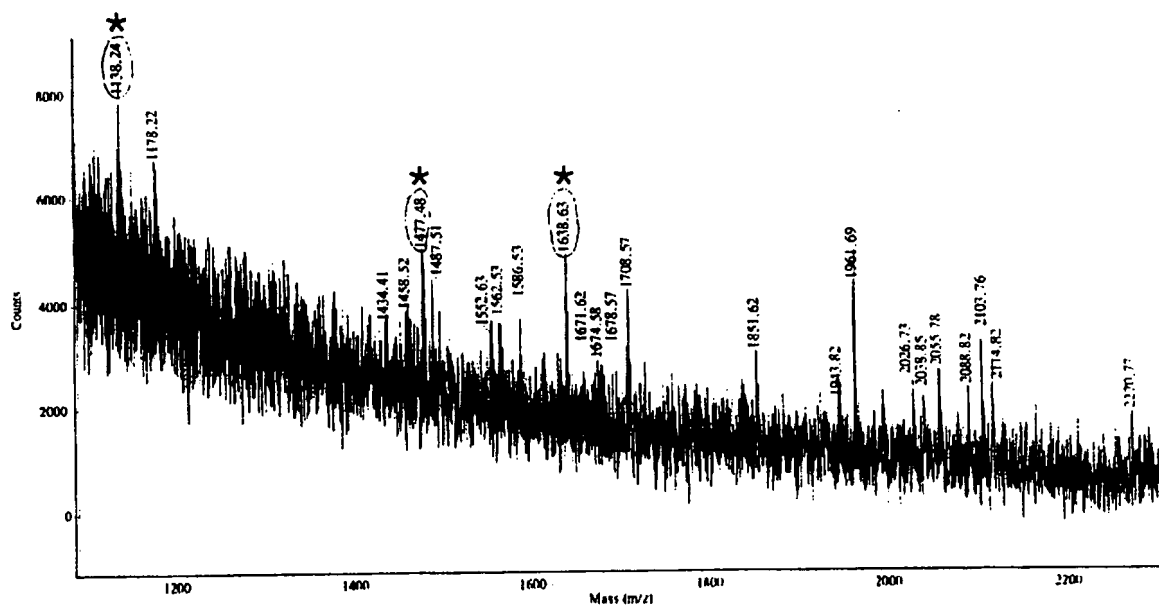


Fig. 12

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 97/02394

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 G01N33/574 G01N33/68 C07K14/47 G01N33/577

According to International Patent Classification(IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 G01N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>I. BYRJALSEN ET AL.: "Human endometrial proteins with cyclic changes in the expression during the normal menstrual cycle: characterization by protein sequence analysis."</p> <p>HUMAN REPRODUCTION, vol. 10, no. 10, 1 October 1995, OXFORD UK, pages 2760-2766, XP002048682 cited in the application see tables 1,2</p> <p style="text-align: center;">--- -/--</p>	<p>1,2,7,8, 13-15</p>

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

1 December 1997

Date of mailing of the international search report

12/12/1997

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Van Bohemen, C

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 97/02394

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	I. BYRJALSEN ET AL.: "Two-dimensional gel analysis of human endometrial proteins: cyclic changes in the expression of specific proteins during the normal menstrual cycle." HUMAN REPRODUCTION, vol. 10, no. 1, 1 January 1995, OXFORD UK, pages 13-18, XP002048683 cited in the application see the whole document	1
Y	----	2-16
Y	WO 94 28021 A (MEDICAL UNIVERSITY OF SOUTH CAROLINA) 8 December 1994 see page 3, line 10 - line 5; claims 4,17 ----	2-16
X	W.B. NOTHNICK ET AL.: "Detection of a unique 32-kd protein in the peritoneal fluid of women with endometriosis." FERTILITY AND STERILITY, vol. 61, no. 2, 1 February 1994, WASHINGTON DC USA, pages 288-293, XP002048684 see figure 2 ----	1-3,13
A	K.L. SHARPE ET AL.: "Polypeptides synthesized and released by human endometriosis differ from those of the uterine endometrium in cell and tissue explant culture." FERTILITY AND STERILITY, vol. 60, no. 5, 1 November 1993, WASHINGTON DC USA, pages 839-851, XP002048685 see figures 1,2 -----	1-16

Information on patent family members

PCT/GB 97/02394

Form PCT/ISA/210 (patent family annex) (July 1992)